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- (71) Applicants: CHIRON CORPORATION [US/US]; 4560 Horton Street - R440, Emeryville, CA 94608 (US). HYSEQ INC. [US/US]; 675 Almanor Avenue, Sunnyvale, CA 94086 (US).
- (72) Inventors: WILLIAMS, Lewis, T.; 3 Miroflores, Tiburon, CA 94920 (US). ESCOBEDO, Jaime; 1470 Lavorna Road, Alamo, CA 94507 (US). INNIS, Michael, A.; 315 Constance Place, Moraga, CA 94556 (US). GARCIA, Pablo, Dominguez; 882 Chenery Street, San Francisco, CA 94131 (US). SUDDUTH-KLINGER, Julie; 280 Lexington Road, Kensington, CA 94707 (US). REINHARD, Christoph; 1633 Clinton Avenue, Alameda, CA 94501 (US). GIESE, Klaus; Chausseetrabe 92, D-10115 Berlin (DE). RANDAZZO, Filippo; Apt. 403, 690 Chestnut Street, San Francisco, CA 94133 (US). KENNEDY, Giulia, C.; 360 Castenada Av-

enue, San Francisco, CA 94116 (US). POT, David; 1565 5th Avenue #102, San Francisco, CA 94112 (US). KASSAM, Altaf; 2659 Harold Street, Oakland, CA 94602 (US). LAM-SON, George; 232 Sandringham Drive, Moraga, CA 94556 (US). DRMANAC, Radoje; 850 East Greenwich Place, Palo Alto, CA 94303 (US). CRKVENJAKOV, Radomir; 762 Haverhill Drive, Sunnyvale, CA 94068 (US). DICKSON, Mark; 1411 Gabilan Drive #B, Hollister, CA 95025 (US). DRMANAC, Snezana; 850 East Greenwich Place, Palo Alto, CA 94303 (US). LABAT, Ivan; 140 Acalanes Drive, Sunnyvale, CA 94086 (US). LESHKOWITZ, Dena; 678 Durshire Way, Sunnyvale, CA 94087 (US). KITA, David; 899 Bounty Drive, Foster City, CA 94404 (US). GARCIA, Veronica; Apartment 412, 396 Ano Nuevo, Sunnyvale, CA 94086 (US). JONES, Lee, William; 396 Ano Nuevo #412, Sunnyvale, CA 94086 (US). STACHE-CRAIN, Birgit; 345 South Mary Avenue, Sunnyvale, CA 94086 (US).

- (74) Agent: BLACKBURN, Robert, P.; Chiron Corporation, P.O. Box 8097, Emeryville, CA 94662–8097 (US).
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(57) Abstract

This invention relates to novel human polynucleotides and variants thereof, their encoded polypeptides and variants thereof, to genes corresponding to these polynucleotides and to proteins expressed by the genes. The invention also relates to diagnostic and therapeutic agents employing such novel human polynucleotides, their corresponding genes or gene products, e.g., these genes and proteins, including probes, antisense constructs, and antibodies.

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Cross-References to Related Applications

This application is a continuation-in-part of U.S. provisional patent application serial no. 60/068,755, filed December 23, 1997, and of U.S. provisional patent application serial no. 60/080,664, filed April 3, 1998, and of U.S. provisional patent application serial no. 60/105,234, filed October 21, 1998, each of which applications are incorporated herein by reference.

10 Field of the Invention

The present invention relates to novel polynucleotides, particularly to novel polynucleotides of human origin that are expressed in a selected cell type, are differentially expressed in one cell type relative to another cell type (e.g., in cancerous cells, or in cells of a specific tissue origin) and/or share homology to polynucleotides encoding a gene product having an identified functional domain and/or activity.

Background of the Invention

Identification of novel polynucleotides, particularly those that encode an expressed gene product, is important in the advancement of drug discovery, diagnostic technologies, and the understanding of the progression and nature of complex diseases such as cancer. Identification of genes expressed in different cell types isolated from sources that differ in disease state or stage, developmental stage, exposure to various environmental factors, the tissue of origin, the species from which the tissue was isolated, and the like is key to identifying the genetic factors that are responsible for the phenotypes associated with these various differences

This invention provides novel human polynucleotides, the polypeptides encoded by these polynucleotides, and the genes and proteins corresponding to these novel polynucleotides.

30 Summary of the Invention

This invention relates to novel human polynucleotides and variants thereof, their encoded polypeptides and variants thereof, to genes corresponding to these polynucleotides

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WO 99/33982 PCT/US98/27610 and to proteins expressed by the genes. The invention also relates to diagnostic and therapeutic agents employing such novel human polynucleotides, their corresponding genes or gene products, *e.g.*, these genes and proteins, including probes, antisense constructs, and antibodies.

Accordingly, in one embodiment, the present invention features a library of polynucleotides, the library comprising the sequence information of at least one of SEQ ID NOS:1-844. In related aspects, the invention features a library provided on a nucleic acid array, or in a computer-readable format.

In one embodiment, the library is comprises a differentially expressed polynucleotide 10 comprising a sequence selected from the group consisting of SEQ ID NOS:9, 39, 42, 52, 62, 74, 119, 172, 317, and 379. In specific related embodiments, the library comprises: 1) a polynucleotide that is differentially expressed in a human breast cancer cell, where the polynucleotide comprises a sequence selected from the group consisting of SEO ID NOS: 4. 9, 39, 42, 52, 62, 65, 66, 68, 74, 81, 114, 123, 144, 130, 157, 162, 172, 178, 183, 202, 214, 15 219, 223, 258, 298, 317, 338, 379, 384, 386, and 388; 2) a polynucleotide differentially expressed in a human colon cancer cell, where the polynucleotide comprises a sequence selected from the group consisting of SEQ ID NOS: 1, 39, 52, 97, 119, 134, 172, 176, 241, 288, 317, 357, 362, and 374; or 3) a polynucleotide differentially expressed in a human lung cancer cell, where the polynucleotide comprises a sequence selected from the group 20 consisting of SEQ ID NOS: 9, 34, 42, 62, 74, 106, 119, 135, 154, 160, 260, 308, 323, 349, 361, 369, 371, 379, 395, 381, and 400.

In another aspect, the invention features an isolated polynucleotide comprising a nucleotide sequence having at least 90% sequence identity to an identifying sequence of SEQ ID NOS:1-844 or a degenerate variant thereof. In related aspects, the invention features recombinant host cells and vectors comprising the polynucleotides of the invention, as well as isolated polypeptides encoded by the polynucleotides of the invention and antibodies that specifically bind such polypeptides.

In one embodiment, the invention features an isolated polynucleotide comprising a sequence encoding a polypeptide of a protein family selected from the group consisting of: 4 transmembrane segments integral membrane proteins, 7 transmembrane receptors, ATPases associated with various cellular activities (AAA), eukaryotic aspartyl proteases,

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GATA family of transcription factors, G-protein alpha subunit, phorbol esters/diacylglycerol binding proteins, protein kinase, protein phosphatase 2C, protein tyrosine phosphatase, trypsin, wnt family of developmental signaling proteins, and WW/rsp5/WWP domain containing proteins. In a specific related embodiment, the invention features a polynucleotide comprising a sequence of one of SEQ ID NOS: 24, 41, 101, 157, 291, 305, 315, 341, 63, 116, 134, 136, 151, 384, 404, 308, 213, 367, 188, 251, 202, 315, 367, 397, 256, 382, 169, 23, 291, 324, 330, 341, 353, 188, 379, and 395.

In another embodiment, the invention features a polynucleotide comprising a sequence encoding a polypeptide having a functional domain selected from the group consisting of: Ank repeat, basic region plus leucine zipper transcription factors, bromodomain, EF-hand, SH3 domain, WD domain/G-beta repeats, zinc finger (C2H2 type), zinc finger (CCHC class), and zinc-binding metalloprotease domain. In a specific related embodiment, the invention features a polynucleotide comprising a sequence of one of SEQ ID NOS: 116, 251, 374, 97, 136, 242, 379, 306, 386, 18, 335, 61, 306, 386, 322, 306, and 395.

In another aspect, the invention features a method of detecting differentially expressed genes correlated with a cancerous state of a mammalian cell, where the method comprises the step of detecting at least one differentially expressed gene product in a test sample derived from a cell suspected of being cancerous, where the gene product is encoded by a gene corresponding to a sequence of at least one of SEQ ID NOS:4, 9, 39, 42, 52, 62, 65, 66, 68, 74, 81, 114, 123, 144, 130, 157, 162, 172, 178, 183, 202, 214, 219, 223, 258, 298, 317, 338, 379, 384, 386, 388, 1, 39, 52, 97, 119, 134, 172, 176, 241, 288, 317, 357, 362, 374, 9, 34, 42, 62, 74, 106, 119, 135, 154, 160, 260, 308, 323, 349, 361, 369, 371, 379, 395, 381, and 400. Detection of the differentially expressed gene product is correlated with a cancerous state of the cell from which the test sample was derived. In one embodiment, the detecting is by hybridization of the test sample to a reference array, wherein the reference array comprises an identifying sequence of at least one of SEQ ID NOS:1-844.

In one embodiment of the method of the invention, the cell is a breast tissue derived cell, and the differentially expressed gene product is encoded by a gene corresponding to a sequence of at least one of SEQ ID NOS: 4, 9, 39, 42, 52, 62, 65, 66, 68, 74, 81, 114, 123,

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In another embodiment of the method of the invention, the cell is a colon tissue derived cell, and differentially expressed gene product is encoded by a gene corresponding to a sequence of at least one of SEQ ID NOS: 1, 39, 52, 97, 119, 134, 172, 176, 241, 288, 317, 357, 362, and 374.

In yet another embodiment of the method of the invention, the cell is a lung tissue derived cell, and differentially expressed gene product is encoded by a gene corresponding to a sequence of at least one of SEQ ID NOS: 9, 34, 42, 62, 74, 106, 119, 135, 154, 160, 260, 308, 323, 349, 361, 369, 371, 379, 395, 381, and 400.

Other aspects and embodiments of the invention will be readily apparent to the ordinarily skilled artisan upon reading the description provided herein.

Detailed Description of the Invention

The invention relates to polynucleotides comprising the disclosed nucleotide sequences, to full length cDNA, mRNA and genes corresponding to these sequences, and to polypeptides and proteins encoded by these polynucleotides and genes.

Also included are polynucleotides that encode polypeptides and proteins encoded by the polynucleotides of the Sequence Listing. The various polynucleotides that can encode these polypeptides and proteins differ because of the degeneracy of the genetic code, in that most amino acids are encoded by more than one triplet codon. The identity of such codons is well-known in this art, and this information can be used for the construction of the polynucleotides within the scope of the invention.

Polynucleotides encoding polypeptides and proteins that are variants of the polypeptides and proteins encoded by the polynucleotides and related cDNA and genes are also within the scope of the invention. The variants differ from wild type protein in having one or more amino acid substitutions that either enhance, add, or diminish a biological activity of the wild type protein. Once the amino acid change is selected, a polynucleotide encoding that variant is constructed according to the invention.

The following detailed description describes the polynucleotide compositions encompassed by the invention, methods for obtaining cDNA or genomic DNA encoding a full-length gene product, expression of these polynucleotides and genes, identification of

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structural motifs of the polynucleotides and genes, identification of the function of a gene product encoded by a gene corresponding to a polynucleotide of the invention, use of the provided polynucleotides as probes and in mapping and in tissue profiling, use of the corresponding polypeptides and other gene products to raise antibodies, and use of the polynucleotides and their encoded gene products for therapeutic and diagnostic purposes.

I. Polynucleotide Compositions

The scope of the invention with respect to polynucleotide compositions includes, but is not necessarily limited to, polynucleotides having a sequence set forth in any one of SEQ ID NOS:1-844; polynucleotides obtained from the biological materials described herein or other biological sources (particularly human sources) by hybridization under stringent conditions (particularly conditions of high stringency); genes corresponding to the provided polynucleotides; variants of the provided polynucleotides and their corresponding genes, particularly those variants that retain a biological activity of the encoded gene product (*e.g.*, a biological activity ascribed to a gene product corresponding to the provided polynucleotides as a result of the assignment of the gene product to a protein family(ies) and/or identification of a functional domain present in the gene product). Other nucleic acid compositions contemplated by and within the scope of the present invention will be readily apparent to one of ordinary skill in the art when provided with the disclosure here.

The invention features polynucleotides that are expressed in cells of human tissue, specifically human colon, breast, and/or lung tissue. Novel nucleic acid compositions of the invention of particular interest comprise a sequence set forth in any one of SEQ ID NOS:1-844 or an identifying sequence thereof. An "identifying sequence" is a contiguous sequence of residues at least about 10 nt to about 20 nt in length, usually at least about 50 nt to about 100 nt in length, that uniquely identifies a polynucleotide sequence, *e.g.*, exhibits less than 90%, usually less than about 80% to about 85% sequence identity to any contiguous nucleotide sequence of more than about 20 nt. Thus, the subject novel nucleic acid compositions include full length cDNAs or mRNAs that encompass an identifying sequence of contiguous nucleotides from any one of SEQ ID NOS:1-844.

The polynucleotides of the invention also include polynucleotides having sequence similarity or sequence identity. Nucleic acids having sequence similarity are detected by

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hybridization under low stringency conditions, for example, at 50°C and 10XSSC (0.9 M saline/0.09 M sodium citrate) and remain bound when subjected to washing at 55°C in 1XSSC. Sequence identity can be determined by hybridization under stringent conditions, for example, at 50°C or higher and 0.1XSSC (9 mM saline/0.9 mM sodium citrate).

Hybridization methods and conditions are well known in the art, see, *e.g.*, U.S. Patent No. 5,707,829. Nucleic acids that are substantially identical to the provided polynucleotide sequences, *e.g.* allelic variants, genetically altered versions of the gene, *etc.*, bind to the provided polynucleotide sequences (SEQ ID NOS:1-844) under stringent hybridization conditions. By using probes, particularly labeled probes of DNA sequences, one can isolate homologous or related genes. The source of homologous genes can be any species, *e.g.* primate species, particularly human; rodents, such as rats and mice, canines, felines, bovines, ovines, equines, yeast, nematodes, *etc.*

Preferably, hybridization is performed using at least 15 contiguous nucleotides of at least one of SEQ ID NOS: 1-844. That is, when at least 15 contiguous nucleotides of one of the disclosed SEQ ID NOs. is used as a probe, the probe will preferentially hybridize with a gene or mRNA (of the biological material) comprising the complementary sequence, allowing the identification and retrieval of the nucleic acids of the biological material that uniquely hybridize to the selected probe. Probes from more than one SEQ ID NO. will hybridize with the same gene or mRNA if the cDNA from which they were derived corresponds to one mRNA. Probes of more than 15 nucleotides can be used, but 15 nucleotides represents enough sequence for unique identification.

The polynucleotides of the invention also include naturally occurring variants of the nucleotide sequences (*e.g.*, degenerate variants, allelic variants, *etc.*). Variants of the polynucleotides of the invention are identified by hybridization of putative variants with nucleotide sequences disclosed herein, preferably by hybridization under stringent conditions. For example, by using appropriate wash conditions, variants of the polynucleotides of the invention can be identified where the allelic variant exhibits at most about 25-30% base pair mismatches relative to the selected polynucleotide probe. In general, allelic variants contain 15-25% base pair mismatches, and can contain as little as even 5-15%, or 2-5%, or 1-2% base pair mismatches, as well as a single base-pair mismatch.

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The invention also encompasses homologs corresponding to the polynucleotides of SEQ ID NOS:1-844, where the source of homologous genes can be any mammalian species, *e.g.*, primate species, particularly human; rodents, such as rats, canines, felines, bovines, ovines, equines, yeast, nematodes, etc. Between mammalian species, *e.g.*, human and mouse, homologs have substantial sequence similarity, *e.g.*, at least 75% sequence identity, usually at least 90%, more usually at least 95% between nucleotide sequences. Sequence similarity is calculated based on a reference sequence, which may be a subset of a larger sequence, such as a conserved motif, coding region, flanking region, *etc.* A reference sequence will usually be at least about 18 contiguous nt long, more usually at least about 30 nt long, and may extend to the complete sequence that is being compared. Algorithms for sequence analysis are known in the art, such as BLAST, described in Altschul *et al.*, *J. Mol. Biol.* (1990) 215:403-10.

In general, variants of the invention have a sequence identity greater than at least about 65%, preferably at least about 75%, more preferably at least about 85%, and can be greater than at least about 90% or more as determined by the Smith-Waterman homology search algorithm as implemented in MPSRCH program (Oxford Molecular). For the purposes of this invention, a preferred method of calculating percent identity is the Smith-Waterman algorithm, using the following. Global DNA sequence identity must be greater than 65% as determined by the Smith-Waterman homology search algorithm as implemented in MPSRCH program (Oxford Molecular) using an affine gap search with the following search parameters: gap open penalty, 12; and gap extension penalty, 1.

The subject nucleic acids can be cDNAs or genomic DNAs, as well as fragments thereof, particularly fragments that encode a biologically active gene product and/or are useful in the methods disclosed herein (e.g., in diagnosis, as a unique identifier of a differentially expressed gene of interest, etc.). The term "cDNA" as used herein is intended to include all nucleic acids that share the arrangement of sequence elements found in native mature mRNA species, where sequence elements are exons and 3 and 5 non-coding regions. Normally mRNA species have contiguous exons, with the intervening introns, when present, being removed by nuclear RNA splicing, to create a continuous open reading frame encoding a polypeptide of the invention.

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A genomic sequence of interest comprises the nucleic acid present between the initiation codon and the stop codon, as defined in the listed sequences, including all of the introns that are normally present in a native chromosome. It can further include the 3 and 5 untranslated regions found in the mature mRNA. It can further include specific transcriptional and translational regulatory sequences, such as promoters, enhancers, *etc.*, including about 1 kb, but possibly more, of flanking genomic DNA at either the 5 and 3 end of the transcribed region. The genomic DNA can be isolated as a fragment of 100 kbp or smaller; and substantially free of flanking chromosomal sequence. The genomic DNA flanking the coding region, either 3 and 5, or internal regulatory sequences as sometimes found in introns, contains sequences required for proper tissue, stage-specific, or disease-state specific expression.

The nucleic acid compositions of the subject invention can encode all or a part of the subject differentially expressed polypeptides. Double or single stranded fragments can be obtained from the DNA sequence by chemically synthesizing oligonucleotides in accordance with conventional methods, by restriction enzyme digestion, by PCR amplification, *etc*. Isolated polynucleotides and polynucleotide fragments of the invention comprise at least about 10, about 15, about 20, about 35, about 50, about 100, about 150 to about 200, about 250 to about 300, or about 350 contiguous nucleotides selected from the polynucleotide sequences as shown in SEQ ID NOS:1-844. For the most part, fragments will be of at least 15 nt, usually at least 18 nt or 25 nt, and up to at least about 50 contiguous nt in length or more. In a preferred embodiment, the polynucleotide molecules comprise a contiguous sequence of at least twelve nucleotides selected from the group consisting of the polynucleotides shown in SEQ ID NOS:1-844.

Probes specific to the polynucleotides of the invention can be generated using the polynucleotide sequences disclosed in SEQ ID NOS:1-844. The probes are preferably at least about 12, 15, 16, 18, 20, 22, 24, or 25 nucleotide fragment of a corresponding contiguous sequence of SEQ ID NOS:1-844, and can be less than 2, 1, 0.5, 0.1, or 0.05 kb in length. The probes can be synthesized chemically or can be generated from longer polynucleotides using restriction enzymes. The probes can be labeled, for example, with a radioactive, biotinylated, or fluorescent tag. Preferably, probes are designed based upon an identifying sequence of a polynucleotide of one of SEQ ID NOS:1-844. More preferably,

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probes are designed based on a contiguous sequence of one of the subject polynucleotides that remain unmasked following application of a masking program for masking low complexity (e.g., XBLAST) to the sequence., i.e., one would select an unmasked region, as indicated by the polynucleotides outside the poly-n stretches of the masked sequence produced by the masking program.

The polynucleotides of the subject invention are isolated and obtained in substantial purity, generally as other than an intact chromosome. Usually, the polynucleotides, either as DNA or RNA, will be obtained substantially free of other naturally-occurring nucleic acid sequences, generally being at least about 50%, usually at least about 90% pure and are typically "recombinant", *e.g.*, flanked by one or more nucleotides with which it is not normally associated on a naturally occurring chromosome.

The polynucleotides of the invention can be provided as a linear molecule or within a circular molecule. They can be provided within autonomously replicating molecules (vectors) or within molecules without replication sequences. They can be regulated by their own or by other regulatory sequences, as is known in the art. The polynucleotides of the invention can be introduced into suitable host cells using a variety of techniques which are available in the art, such as transferrin polycation-mediated DNA transfer, transfection with naked or encapsulated nucleic acids, liposome-mediated DNA transfer, intracellular transportation of DNA-coated latex beads, protoplast fusion, viral infection, electroporation, gene gun, calcium phosphate-mediated transfection, and the like.

The subject nucleic acid compositions can be used to, for example, produce polypeptides, as probes for the detection of mRNA of the invention in biological samples (e.g., extracts of human cells) to generate additional copies of the polynucleotides, to generate ribozymes or antisense oligonucleotides, and as single stranded DNA probes or as triple-strand forming oligonucleotides. The probes described herein can be used to, for example, determine the presence or absence of the polynucleotide sequences as shown in SEQ ID NOS:1-844 or variants thereof in a sample. These and other uses are described in more detail below.

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Use of Polynucleotides to Obtain Full-Length cDNA and Full-Length Human Gene and
Promoter Region

Full-length cDNA molecules comprising the disclosed polynucleotides are obtained as follows. A polynucleotide having a sequence of one of SEQ ID NOS:1-844, or a portion thereof comprising at least 12, 15, 18, or 20 nucleotides, is used as a hybridization probe to 5 detect hybridizing members of a cDNA library using probe design methods, cloning methods, and clone selection techniques such as those described in U.S. Patent No. 5,654,173. Libraries of cDNA are made from selected tissues, such as normal or tumor tissue, or from tissues of a mammal treated with, for example, a pharmaceutical agent. 10 Preferably, the tissue is the same as the tissue from which the polynucleotides of the invention were isolated, as both the polynucleotides described herein and the cDNA represent expressed genes. Most preferably, the cDNA library is made from the biological material described herein in the Examples. Alternatively, many cDNA libraries are available commercially. (Sambrook et al., Molecular Cloning: A Laboratory Manual, 2nd Ed., (1989) 15 Cold Spring Harbor Press, Cold Spring Harbor, NY). The choice of cell type for library construction can be made after the identity of the protein encoded by the gene corresponding to the polynucleotide of the invention is known. This will indicate which tissue and cell types are likely to express the related gene, and thus represent a suitable source for the mRNA for generating the cDNA. Where the provided polynucleotides are isolated from 20 cDNA libraries, the libraries are prepared from mRNA of human colon cells, more preferably, human colon cancer cells, even more preferably, from a highly metastatic colon cell, Km12L4-A.

Techniques for producing and probing nucleic acid sequence libraries are described, for example, in Sambrook *et al.*, *Molecular Cloning: A Laboratory Manual, 2nd Ed.*, (1989)

Cold Spring Harbor Press, Cold Spring Harbor, NY. The cDNA can be prepared by using primers based on sequence from SEQ ID NOS:1-844. In one embodiment, the cDNA library can be made from only poly-adenylated mRNA. Thus, poly-T primers can be used to prepare cDNA from the mRNA.

Members of the library that are larger than the provided polynucleotides, and preferably that encompass the complete coding sequence of the native message, are obtained. In order to confirm that the entire cDNA has been obtained, RNA protection experiments

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are performed as follows. Hybridization of a full-length cDNA to an mRNA will protect the RNA from RNase degradation. If the cDNA is not full length, then the portions of the mRNA that are not hybridized will be subject to RNase degradation. This is assayed, as is known in the art, by changes in electrophoretic mobility on polyacrylamide gels, or by detection of released monoribonucleotides. Sambrook *et al.*, *Molecular Cloning: A Laboratory Manual*, *2nd Ed.*, (1989) Cold Spring Harbor Press, Cold Spring Harbor, NY. In order to obtain additional sequences 5' to the end of a partial cDNA, 5' RACE (*PCR Protocols: A Guide to Methods and Applications*, (1990) Academic Press, Inc.) is performed.

Genomic DNA is isolated using the provided polynucleotides in a manner similar to the isolation of full-length cDNAs. Briefly, the provided polynucleotides, or portions thereof, are used as probes to libraries of genomic DNA. Preferably, the library is obtained from the cell type that was used to generate the polynucleotides of the invention, but this is not essential. Most preferably, the genomic DNA is obtained from the biological material described herein in the Examples. Such libraries can be in vectors suitable for carrying large segments of a genome, such as P1 or YAC, as described in detail in Sambrook *et al.*, 9.4-9.30. In addition, genomic sequences can be isolated from human BAC libraries, which are commercially available from Research Genetics, Inc., Huntville, Alabama, USA, for example. In order to obtain additional 5' or 3' sequences, chromosome walking is performed, as described in Sambrook *et al.*, such that adjacent and overlapping fragments of genomic DNA are isolated. These are mapped and pieced together, as is known in the art, using restriction digestion enzymes and DNA ligase.

Using the polynucleotide sequences of the invention, corresponding full-length genes can be isolated using both classical and PCR methods to construct and probe cDNA libraries. Using either method, Northern blots, preferably, are performed on a number of cell types to determine which cell lines express the gene of interest at the highest level. Classical methods of constructing cDNA libraries are taught in Sambrook *et al.*, *supra*. With these methods, cDNA can be produced from mRNA and inserted into viral or expression vectors. Typically, libraries of mRNA comprising poly(A) tails can be produced with poly(T) primers. Similarly, cDNA libraries can be produced using the instant sequences as primers.

PCR methods are used to amplify the members of a cDNA library that comprise the desired insert. In this case, the desired insert will contain sequence from the full length

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cDNA that corresponds to the instant polynucleotides. Such PCR methods include gene trapping and RACE methods. Gene trapping entails inserting a member of a cDNA library into a vector. The vector then is denatured to produce single stranded molecules. Next, a substrate-bound probe, such a biotinylated oligo, is used to trap cDNA inserts of interest.

Biotinylated probes can be linked to an avidin-bound solid substrate. PCR methods can be used to amplify the trapped cDNA. To trap sequences corresponding to the full length genes, the labeled probe sequence is based on the polynucleotide sequences of the invention. Random primers or primers specific to the library vector can be used to amplify the trapped cDNA. Such gene trapping techniques are described in Gruber *et al.*, WO 95/04745 and Gruber *et al.*, U.S. Pat. No. 5,500,356. Kits are commercially available to perform gene trapping experiments from, for example, Life Technologies, Gaithersburg, Maryland, USA.

"Rapid amplification of cDNA ends," or RACE, is a PCR method of amplifying cDNAs from a number of different RNAs. The cDNAs are ligated to an oligonucleotide linker, and amplified by PCR using two primers. One primer is based on sequence from the instant polynucleotides, for which full length sequence is desired, and a second primer comprises sequence that hybridizes to the oligonucleotide linker to amplify the cDNA. A description of this methods is reported in WO 97/19110. In preferred embodiments of RACE, a common primer is designed to anneal to an arbitrary adaptor sequence ligated to cDNA ends (Apte and Siebert, *Biotechniques* (1993) 15:890-893; Edwards et al., Nuc. Acids Res. (1991) 19:5227-5232). When a single gene-specific RACE primer is paired with the common primer, preferential amplification of sequences between the single gene specific primer and the common primer occurs. Commercial cDNA pools modified for use in RACE are available.

Another PCR-based method generates full-length cDNA library with anchored ends without needing specific knowledge of the cDNA sequence. The method uses lock-docking primers (I-VI), where one primer, poly TV (I-III) locks over the polyA tail of eukaryotic mRNA producing first strand synthesis and a second primer, polyGH (IV-VI) locks onto the polyC tail added by terminal deoxynucleotidyl transferase (TdT). This method is described in WO 96/40998.

The promoter region of a gene generally is located 5' to the initiation site for RNA polymerase II. Hundreds of promoter regions contain the "TATA" box, a sequence such as

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TATTA or TATAA, which is sensitive to mutations. The promoter region can be obtained by performing 5' RACE using a primer from the coding region of the gene. Alternatively, the cDNA can be used as a probe for the genomic sequence, and the region 5' to the coding region is identified by "walking up." If the gene is highly expressed or differentially expressed, the promoter from the gene can be of use in a regulatory construct for a heterologous gene.

Once the full-length cDNA or gene is obtained, DNA encoding variants can be prepared by site-directed mutagenesis, described in detail in Sambrook *et al.*, 15.3-15.63. The choice of codon or nucleotide to be replaced can be based on disclosure herein on optional changes in amino acids to achieve altered protein structure and/or function.

As an alternative method to obtaining DNA or RNA from a biological material, nucleic acid comprising nucleotides having the sequence of one or more polynucleotides of the invention can be synthesized. Thus, the invention encompasses nucleic acid molecules ranging in length from 15 nucleotides (corresponding to at least 15 contiguous nucleotides of one of SEQ ID NOS: 1-844) up to a maximum length suitable for one or more biological manipulations, including replication and expression, of the nucleic acid molecule. The invention includes but is not limited to (a) nucleic acid having the size of a full gene, and comprising at least one of SEQ ID NOS: 1-844; (b) the nucleic acid of (a) also comprising at least one additional gene, operably linked to permit expression of a fusion protein; (c) an expression vector comprising (a) or (b); (d) a plasmid comprising (a) or (b); and (e) a recombinant viral particle comprising (a) or (b). Once provided with the polynucleotides disclosed herein, construction or preparation of (a) - (e) are well within the skill in the art.

The sequence of a nucleic acid comprising at least 15 contiguous nucleotides of at least any one of SEQ ID NOS: 1-844, preferably the entire sequence of at least any one of SEQ ID NOS: 1-844, is not limited and can be any sequence of A, T, G, and/or C (for DNA) and A, U, G, and/or C (for RNA) or modified bases thereof, including inosine and pseudouridine. The choice of sequence will depend on the desired function and can be dictated by coding regions desired, the intron-like regions desired, and the regulatory regions desired. Where the entire sequence of any one of SEQ ID NOS: 1-844 is within the nucleic acid, the nucleic acid obtained is referred to herein as a polynucleotide comprising the sequence of any one of SEQ ID NOS: 1-844.

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II. Expression of Polypeptide Encoded by Full-Length cDNA or Full-Length Gene
 The provided polynucleotide (e.g., a polynucleotide having a sequence of one of SEQ
 ID NOS:1-844), the corresponding cDNA, or the full-length gene is used to express a partial or complete gene product.

Constructs of polynucleotides having sequences of SEQ ID NOS:1-844 can be generated synthetically. Alternatively, single-step assembly of a gene and entire plasmid from large numbers of oligodeoxyribonucleotides is described by, *e.g.*, Stemmer *et al.*, *Gene (Amsterdam)* (1995) 164(1):49-53. In this method, assembly PCR (the synthesis of long DNA sequences from large numbers of oligodeoxyribonucleotides (oligos)) is described. The method is derived from DNA shuffling (Stemmer, *Nature* (1994) 370:389-391), and does not rely on DNA ligase, but instead relies on DNA polymerase to build increasingly longer DNA fragments during the assembly process. For example, a 1.1-kb fragment containing the TEM-1 beta-lactamase-encoding gene (bla) can be assembled in a single reaction from a total of 56 oligos, each 40 nucleotides (nt) in length. The synthetic gene can be PCR amplified and cloned in a vector containing the tetracycline-resistance gene (Tc-R) as the sole selectable marker. Without relying on ampicillin (Ap) selection, 76% of the Tc-R colonies were Ap-R, making this approach a general method for the rapid and cost-effective synthesis of any gene.

Appropriate polynucleotide constructs are purified using standard recombinant DNA techniques as described in, for example, Sambrook *et al.*, *Molecular Cloning: A Laboratory Manual, 2nd Ed.*, (1989) Cold Spring Harbor Press, Cold Spring Harbor, NY, and under current regulations described in United States Dept. of HHS, National Institute of Health (NIH) Guidelines for Recombinant DNA Research. The gene product encoded by a polynucleotide of the invention is expressed in any expression system, including, for example, bacterial, yeast, insect, amphibian and mammalian systems. Suitable vectors and host cells are described in U.S. Patent No. 5,654,173.

Bacteria. Expression systems in bacteria include those described in Chang et al., Nature (1978) 275:615; Goeddel et al., Nature (1979) 281:544; Goeddel et al., Nucleic Acids Res. (1980) 8:4057; EP 0 036,776; U.S. Patent No. 4,551,433; DeBoer et al., Proc. Natl. Acad. Sci. (USA) (1983) 80:21-25; and Siebenlist et al., Cell (1980) 20:269.

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Yeast. Expression systems in yeast include those described in Hinnen et al., Proc. Natl. Acad. Sci. (USA) (1978) 75:1929; Ito et al., J. Bacteriol. (1983) 153:163; Kurtz et al., Mol. Cell. Biol. (1986) 6:142; Kunze et al., J. Basic Microbiol. (1985) 25:141; Gleeson et al., J. Gen. Microbiol. (1986) 132:3459; Roggenkamp et al., Mol. Gen. Genet. (1986)
202:302; Das et al., J. Bacteriol. (1984) 158:1165; De Louvencourt et al., J. Bacteriol. (1983) 154:737; Van den Berg et al., Bio/Technology (1990) 8:135; Kunze et al., J. Basic Microbiol. (1985) 25:141; Cregg et al., Mol. Cell. Biol. (1985) 5:3376; U.S. Patent Nos. 4,837,148 and 4,929,555; Beach and Nurse, Nature (1981) 300:706; Davidow et al., Curr. Genet. (1985) 10:380; Gaillardin et al., Curr. Genet. (1985) 10:49; Ballance et al., Biochem.
Biophys. Res. Commun. (1983) 112:284-289; Tilburn et al., Gene (1983) 26:205-221; Yelton et al., Proc. Natl. Acad. Sci. (USA) (1984) 81:1470-1474; Kelly and Hynes, EMBO J. (1985) 4:475479; EP 0 244,234; and WO 91/00357.

Insect Cells. Expression of heterologous genes in insects is accomplished as described in U.S. Patent No. 4,745,051; Friesen et al., "The Regulation of Baculovirus Gene Expression", in: The Molecular Biology Of Baculoviruses (1986) (W. Doerfler, ed.); EP 0 127,839; EP 0 155,476; and Vlak et al., J. Gen. Virol. (1988) 69:765-776; Miller et al., Ann. Rev. Microbiol. (1988) 42:177; Carbonell et al., Gene (1988) 73:409; Maeda et al., Nature (1985) 315:592-594; Lebacq-Verheyden et al., Mol. Cell. Biol. (1988) 8:3129; Smith et al., Proc. Natl. Acad. Sci. (USA) (1985) 82:8844; Miyajima et al., Gene (1987) 58:273; and Martin et al., DNA (1988) 7:99. Numerous baculoviral strains and variants and corresponding permissive insect host cells from hosts are described in Luckow et al., Bio/Technology (1988) 6:47-55, Miller et al., Generic Engineering (1986) 8:277-279, and Maeda et al., Nature (1985) 315:592-594.

Mammalian Cells. Mammalian expression is accomplished as described in Dijkema et al., EMBO J. (1985) 4:761, Gorman et al., Proc. Natl. Acad. Sci. (USA) (1982) 79:6777, Boshart et al., Cell (1985) 41:521 and U.S. Patent No. 4,399,216. Other features of mammalian expression are facilitated as described in Ham and Wallace, Meth. Enz. (1979) 58:44, Barnes and Sato, Anal. Biochem. (1980) 102:255, U.S. Patent Nos. 4,767,704, 4,657,866, 4,927,762, 4,560,655, WO 90/103430, WO 87/00195, and U.S. RE 30,985.

Polynucleotide molecules comprising a polynucleotide sequence provided herein propagated by placing the molecule in a vector. Viral and non-viral vectors are used,

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including plasmids. The choice of plasmid will depend on the type of cell in which propagation is desired and the purpose of propagation. Certain vectors are useful for amplifying and making large amounts of the desired DNA sequence. Other vectors are suitable for expression in cells in culture. Still other vectors are suitable for transfer and expression in cells in a whole animal or person. The choice of appropriate vector is well within the skill of the art. Many such vectors are available commercially. The partial or full-length polynucleotide is inserted into a vector typically by means of DNA ligase attachment to a cleaved restriction enzyme site in the vector. Alternatively, the desired nucleotide sequence can be inserted by homologous recombination in vivo. Typically this is accomplished by attaching regions of homology to the vector on the flanks of the desired nucleotide sequence. Regions of homology are added by ligation of oligonucleotides, or by polymerase chain reaction using primers comprising both the region of homology and a portion of the desired nucleotide sequence, for example.

The polynucleotides set forth in SEQ ID NOS:1-844 or their corresponding full-length polynucleotides are linked to regulatory sequences as appropriate to obtain the desired expression properties. These can include promoters (attached either at the 5' end of the sense strand or at the 3' end of the antisense strand), enhancers, terminators, operators, repressors, and inducers. The promoters can be regulated or constitutive. In some situations it may be desirable to use conditionally active promoters, such as tissue-specific or developmental stage-specific promoters. These are linked to the desired nucleotide sequence using the techniques described above for linkage to vectors. Any techniques known in the art can be used.

When any of the above host cells, or other appropriate host cells or organisms, are used to replicate and/or express the polynucleotides or nucleic acids of the invention, the resulting replicated nucleic acid, RNA, expressed protein or polypeptide, is within the scope of the invention as a product of the host cell or organism. The product is recovered by any appropriate means known in the art.

Once the gene corresponding to a selected polynucleotide is identified, its expression can be regulated in the cell to which the gene is native. For example, an endogenous gene of a cell can be regulated by an exogenous regulatory sequence as disclosed in U.S. Patent No. 5,641,670.

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III. <u>Identification of Functional and Structural Motifs of Novel Genes</u>

A. <u>Screening Polynucleotide Sequences and Amino Acid Sequences Against Publicly Available Databases</u>

Translations of the nucleotide sequence of the provided polynucleotides, cDNAs or full genes can be aligned with individual known sequences. Similarity with individual sequences can be used to determine the activity of the polypeptides encoded by the polynucleotides of the invention. For example, sequences that show similarity with a chemokine sequence can exhibit chemokine activities. Also, sequences exhibiting similarity with more than one individual sequence can exhibit activities that are characteristic of either or both individual sequences.

The full length sequences and fragments of the polynucleotide sequences of the nearest neighbors can be used as probes and primers to identify and isolate the full length sequence corresponding to provided polynucleotides. The nearest neighbors can indicate a tissue or cell type to be used to construct a library for the full-length sequences corresponding to the provided polynucleotides..

Typically, a selected polynucleotide is translated in all six frames to determine the best alignment with the individual sequences. The sequences disclosed herein in the Sequence Listing are in a 5' to 3' orientation and translation in three frames can be sufficient (with a few specific exceptions as described in the Examples). These amino acid sequences are referred to, generally, as query sequences, which will be aligned with the individual sequences. Databases with individual sequences are described in "Computer Methods for Macromolecular Sequence Analysis" *Methods in Enzymology* (1996) 266, Doolittle, Academic Press, Inc., a division of Harcourt Brace & Co., San Diego, California, USA. Databases include Genbank, EMBL, and DNA Database of Japan (DDBJ).

Query and individual sequences can be aligned using the methods and computer programs described above, and include BLAST, available over the world wide web at http://www.ncbi.nlm.nih.gov/BLAST/. Another alignment algorithm is Fasta, available in the Genetics Computing Group (GCG) package, Madison, Wisconsin, USA, a wholly owned subsidiary of Oxford Molecular Group, Inc. Other techniques for alignment are described in

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wo 99/33982 PCT/US98/27610 utilized to align the sequences. The Smith-Waterman is one type of algorithm that permits gaps in sequence alignments. See *Meth. Mol. Biol.* (1997) 70: 173-187. Also, the GAP program using the Needleman and Wunsch alignment method can be utilized to align sequences. An alternative search strategy uses MPSRCH software, which runs on a MASPAR computer. MPSRCH uses a Smith-Waterman algorithm to score sequences on a massively parallel computer. This approach improves ability to identify sequences that are distantly related matches, and is especially tolerant of small gaps and nucleotide sequence errors. Amino acid sequences encoded by the provided polynucleotides can be used to search both protein and DNA databases.

Results of individual and query sequence alignments can be divided into three categories, high similarity, weak similarity, and no similarity. Individual alignment results ranging from high similarity to weak similarity provide a basis for determining polypeptide activity and/or structure. Parameters for categorizing individual results include: percentage of the alignment region length where the strongest alignment is found, percent sequence identity, and p value.

The percentage of the alignment region length is calculated by counting the number of residues of the individual sequence found in the region of strongest alignment, *e.g.*, contiguous region of the individual sequence that contains the greatest number of residues that are identical to the residues of the corresponding region of the aligned query sequence. This number is divided by the total residue length of the query sequence to calculate a percentage. For example, a query sequence of 20 amino acid residues might be aligned with a 20 amino acid region of an individual sequence. The individual sequence might be identical to amino acid residues 5, 9-15, and 17-19 of the query sequence. The region of strongest alignment is thus the region stretching from residue 9-19, an 11 amino acid stretch. The percentage of the alignment region length is: 11 (length of the region of strongest alignment) divided by (query sequence length) 20 or 55%.

Percent sequence identity is calculated by counting the number of amino acid matches between the query and individual sequence and dividing total number of matches by the number of residues of the individual sequences found in the region of strongest alignment. Thus, the percent identity in the example above would be 10 matches divided by 11 amino acids, or approximately, 90.9%

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P value is the probability that the alignment was produced by chance. For a single alignment, the p value can be calculated according to Karlin *et al.*, *Proc. Natl. Acad. Sci.* (1990) 87:2264 and Karlin *et al.*, *Proc. Natl. Acad. Sci.* (1993) 90. The p value of multiple alignments using the same query sequence can be calculated using an heuristic approach described in Altschul *et al.*, *Nat. Genet.* (1994) 6:119. Alignment programs such as BLAST program can calculate the p value.

Another factor to consider for determining identity or similarity is the location of the similarity or identity. Strong local alignment can indicate similarity even if the length of alignment is short. Sequence identity scattered throughout the length of the query sequence also can indicate a similarity between the query and profile sequences. The boundaries of the region where the sequences align can be determined according to Doolittle, *supra*; BLAST or FAST programs; or by determining the area where sequence identity is highest.

High Similarity. In general, in alignment results considered to be of high similarity, the percent of the alignment region length is typically at least about 55% of total length query sequence; more typically, at least about 58%; even more typically; at least about 60% of the total residue length of the query sequence. Usually, percent length of the alignment region can be as much as about 62%; more usually, as much as about 64%; even more usually, as much as about 66%. Further, for high similarity, the region of alignment, typically, exhibits at least about 75% of sequence identity; more typically, at least about 78%; even more typically; at least about 80% sequence identity. Usually, percent sequence identity can be as much as about 82%; more usually, as much as about 84%; even more usually, as much as about 86%.

The p value is used in conjunction with these methods. If high similarity is found, the query sequence is considered to have high similarity with a profile sequence when the p value is less than or equal to about 10^{-2} ; more usually; less than or equal to about 10^{-3} ; even more usually; less than or equal to about 10^{-4} . More typically, the p value is no more than about 10^{-5} ; more typically; no more than or equal to about 10^{-10} ; even more typically; no more than or equal to about 10^{-15} for the query sequence to be considered high similarity.

Weak Similarity. In general, where alignment results considered to be of weak similarity, there is no minimum percent length of the alignment region nor minimum length of alignment. A better showing of weak similarity is considered when the region of

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alignment is, typically, at least about 15 amino acid residues in length; more typically, at least about 20; even more typically; at least about 25 amino acid residues in length. Usually, length of the alignment region can be as much as about 30 amino acid residues; more usually, as much as about 40; even more usually, as much as about 60 amino acid residues.

Further, for weak similarity, the region of alignment, typically, exhibits at least about 35% of sequence identity; more typically, at least about 40%; even more typically; at least about 45% sequence identity. Usually, percent sequence identity can be as much as about 50%; more usually, as much as about 55%; even more usually, as much as about 60%.

If low similarity is found, the query sequence is considered to have weak similarity with a profile sequence when the p value is usually less than or equal to about 10^{-2} ; more usually; less than or equal to about 10^{-3} ; even more usually; less than or equal to about 10^{-4} . More typically, the p value is no more than about 10^{-5} ; more usually; no more than or equal to about 10^{-10} ; even more usually; no more than or equal to about 10^{-15} for the query sequence to be considered weak similarity.

Similarity Determined by Sequence Identity Alone. Sequence identity alone can be used to determine similarity of a query sequence to an individual sequence and can indicate the activity of the sequence. Such an alignment, preferably, permits gaps to align sequences. Typically, the query sequence is related to the profile sequence if the sequence identity over the entire query sequence is at least about 15%; more typically, at least about 20%; even more typically, at least about 50%. Sequence identity alone as a measure of similarity is most useful when the query sequence is usually, at least 80 residues in length; more usually, 90 residues; even more usually, at least 95 amino acid residues in length. More typically, similarity can be concluded based on sequence identity alone when the query sequence is preferably 100 residues in length; more preferably, 120 residues in length; even more preferably, 150 amino acid residues in length.

Determining Activity from Alignments with Profile and Multiple Aligned Sequences. Translations of the provided polynucleotides can be aligned with amino acid profiles that define either protein families or common motifs. Also, translations of the provided polynucleotides can be aligned to multiple sequence alignments (MSA) comprising the polypeptide sequences of members of protein families or motifs. Similarity or identity with profile sequences or MSAs can be used to determine the activity of the gene products (e.g.,

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polypeptides) encoded by the provided polynucleotides or corresponding cDNA or genes. For example, sequences that show an identity or similarity with a chemokine profile or MSA can exhibit chemokine activities.

Profiles can designed manually by (1) creating an MSA, which is an alignment of the 5 amino acid sequence of members that belong to the family and (2) constructing a statistical representation of the alignment. Such methods are described, for example, in Birney et al., Nucl. Acid Res. (1996) 24(14): 2730-2739. MSAs of some protein families and motifs are publicly available. For example, http://genome.wustl.edu/Pfam/ includes MSAs of 547 different families and motifs. These MSAs are described also in Sonnhammer et al., Proteins (1997) 28: 405-420. Other sources over the world wide web include the site at 10 http://www.embl-heidelberg.de/argos/ali/ali.htm1; alternatively, a message can be sent to ALI@EMBL-HEIDELBERG.DE for the information. A brief description of these MSAs is reported in Pascarella et al., Prot. Eng. (1996) 9(3):249-251. Techniques for building profiles from MSAs are described in Sonnhammer et al., supra; Birney et al., supra; and "Computer Methods for Macromolecular Sequence Analysis," Methods in Enzymology 15 (1996) 266, Doolittle, Academic Press, Inc., a division of Harcourt Brace & Co., San Diego, California, USA.

Similarity between a query sequence and a protein family or motif can be determined by (a) comparing the query sequence against the profile and/or (b) aligning the query sequence with the members of the family or motif. Typically, a program such as Searchwise is used to compare the query sequence to the statistical representation of the multiple alignment, also known as a profile. The program is described in Birney *et al.*, *supra*. Other techniques to compare the sequence and profile are described in Sonnhammer *et al.*, *supra* and Doolittle, *supra*.

Next, methods described by Feng et al., J. Mol. Evol. (1987) 25:351 and Higgins et al., CABIOS (1989) 5:151 can be used align the query sequence with the members of a family or motif, also known as a MSA. Computer programs, such as PILEUP, can be used. See Feng et al., infra. In general, the following factors are used to determine if a similarity between a query sequence and a profile or MSA exists: (1) number of conserved residues found in the query sequence, (2) percentage of conserved residues found in the query sequence, (3) number of frameshifts, and (4) spacing between conserved residues.

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Some alignment programs that both translate and align sequences can make any number of frameshifts when translating the nucleotide sequence to produce the best alignment. The fewer frameshifts needed to produce an alignment, the stronger the similarity or identity between the query and profile or MSAs. For example, a weak similarity resulting from no frameshifts can be a better indication of activity or structure of a query sequence, than a strong similarity resulting from two frameshifts. Preferably, three or fewer frameshifts are found in an alignment; more preferably two or fewer frameshifts; even more preferably, no frameshifts are found in an alignment of query and profile or MSAs.

Conserved residues are those amino acids found at a particular position in all or some of the family or motif members. For example, most chemokines contain four conserved cysteines. Alternatively, a position is considered conserved if only a certain class of amino acids is found in a particular position in all or some of the family members. For example, the N-terminal position can contain a positively charged amino acid, such as lysine, arginine, or histidine.

Typically, a residue of a polypeptide is conserved when a class of amino acids or a single amino acid is found at a particular position in at least about 40% of all class members; more typically, at least about 50%; even more typically, at least about 60% of the members. Usually, a residue is conserved when a class or single amino acid is found in at least about 70% of the members of a family or motif; more usually, at least about 80%; even more usually, at least about 95%.

A residue is considered conserved when three unrelated amino acids are found at a particular position in the some or all of the members; more usually, two unrelated amino acids. These residues are conserved when the unrelated amino acids are found at particular positions in at least about 40% of all class member; more typically, at least about 50%; even more typically, at least about 60% of the members. Usually, a residue is conserved when a class or single amino acid is found in at least about 70% of the members of a family or motif; more usually, at least about 80%; even more usually, at least about 90%; even more usually, at least about 95%.

A query sequence has similarity to a profile or MSA when the query sequence comprises at least about 25% of the conserved residues of the profile or MSA; more usually,

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at least about 30%; even more usually; at least about 40%. Typically, the query sequence has a stronger similarity to a profile sequence or MSA when the query sequence comprises at least about 45% of the conserved residues of the profile or MSA; more typically, at least about 50%; even more typically; at least about 55%.

B. Screening Polynucleotide and Amino Acid Sequences Against Protein Profiles

The identify and function of the gene that correlates to a polynucleotide described herein can be determined by screening the polynucleotides or their corresponding amino acid sequences against profiles of protein families. Such profiles focus on common structural motifs among proteins of each family. Publicly available profiles are described above in Section IVA. Additional or alternative profiles are described below.

In comparing a novel polynucleotide with known sequences, several alignment tools are available. Examples include PileUp, which creates a multiple sequence alignment, and is described in Feng *et al.*, *J. Mol. Evol.* (1987) 25:351. Another method, GAP, uses the alignment method of Needleman *et al.*, *J. Mol. Biol.* (1970) 48:443. GAP is best suited for global alignment of sequences. A third method, BestFit, functions by inserting gaps to maximize the number of matches using the local homology algorithm of Smith *et al.*, *Adv. Appl. Math.* (1981) 2:482. Exemplary protein profiles are provided below and in the examples.

<u>Chemokines.</u> Chemokines are a family of proteins that have been implicated in lymphocyte trafficking, inflammatory diseases, angiogenesis, hematopoiesis, and viral infection. See, for example, Rollins, *Blood* (1997) *90*(*3*):909-928, and Wells *et al.*, *J. Leuk. Biol.* (1997) *61*:545-550. U.S. Patent No. 5,605,817 discloses DNA encoding a chemokine expressed in fetal spleen. U.S. Patent No. 5,656,724 discloses chemokine-like proteins and methods of use. U.S. Patent No. 5,602,008 discloses DNA encoding a chemokine expressed by liver.

Chemokine mutants are polypeptides having an amino acid sequence that possesses at least one amino acid substitution, addition, or deletion as compared to native chemokines. Fragments possess the same amino acid sequence of the native chemokines; mutants can lack the amino and/or carboxyl terminal sequences. Fusions are mutants, fragments, or native chemokines that also include amino and/or carboxyl terminal amino acid extensions.

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The number or type of the amino acid changes is not critical, nor is the length or number of the amino acid deletions, or amino acid extensions that are incorporated in the chemokines as compared to the native chemokine amino acid sequences. A polynucleotide encoding one of these variant polypeptides will retain at least about 80% amino acid identity with at least one known chemokine. Preferably, these polypeptides will retain at least about 85% amino acid sequence identity, more preferably, at least about 90%; even more preferably, at least about 95%. In addition, the variants exhibit at least 80%; preferably about 90%; more preferably about 95% of at least one activity exhibited by a native chemokine, which includes immunological, biological, receptor binding, and signal transduction functions.

Assays for chemotaxis relating to neutrophils are described in Walz et al., Biochem. Biophys. Res. Commun. (1987) 149:755, Yoshimura et al., Proc. Natl. Acad. Sci. (USA) (1987) 84:9233, and Schroder et al., J. Immunol. (1987) 139:3474; to lymphocytes, Larsen et al., Science (1989) 243:1464, Carr et al., Proc. Natl. Acad. Sci. (USA) (1994) 91:3652; to tumor-infiltrating lymphocytes, Liao et al., J. Exp. Med (1995). 182:1301; to hematopoietic progenitors, Aiuti et al., J. Exp. Med. (1997) 185:111; to monocytes, Valente et al., Biochem. (1988) 27:4162; and to natural killer cells, Loetscher et al., J. Immunol. (1996) 156:322, and Allavena et al., Eur. J. Immunol. (1994) 24:3233.

Assays for determining the biological activity of attracting eosinophils are described in Dahinden et al., J. Exp. Med. (1994) 179:751, Weber et al., J. Immunol. (1995) 154:4166, and Noso et al., Biochem. Biophys. Res. Commun. (1994) 200:1470; for attracting dendritic cells, Sozzani et al., J. Immunol. (1995) 155:3292; for attracting basophils, in Dahinden et al., J. Exp. Med. (1994) 179:751, Alam et al., J. Immunol. (1994) 152:1298, Alam et al., J. Exp. Med. (1992) 176:781; and for activating neutrophils, Maghazaci et al., Eur. J. Immunol. (1996) 26:315, and Taub et al., J. Immunol. (1995) 155:3877. Native chemokines can act as mitogens for fibroblasts, assayed as described in Mullenbach et al., J. Biol. Chem. (1986) 261:719.

Native chemokines exhibit binding activity with a number of receptors. Description of such receptors and assays to detect binding are described in, for example, Murphy *et al.*, *Science* (1991) *253*:1280; Combadiere *et al.*, *J. Biol. Chem.* (1995) *270*:29671; Daugherty *et al.*, *J. Exp. Med.* (1996) *183*:2349; Samson *et al.*, *Biochem.* (1996) *35*:3362; Raport *et al.*, *J.*

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Biol. Chem. (1996) 271:17161; Combadiere et al., J. Leukoc. Biol. (1996) 60:147; Baba et al., J. Biol. Chem. (1997) 23:14893; Yosida et al., J. Biol. Chem. (1997) 272:13803; Arvannitakis et al., Nature (1997) 385:347, and other assays are known in the art.

Assays for kinase activation of chemokines are described by Yen et al., J. Leukoc.

Biol. (1997) 61:529; Dubois et al., J. Immunol. (1996) 156:1356; Turner et al., J. Immunol. (1995) 155:2437. Assays for inhibition of angiogenesis or cell proliferation are described in Maione et al., Science (1990) 247:77. Glycosaminoglycan production can be induced by native chemokines, assayed as described in Castor et al., Proc. Natl. Acad. Sci. (USA) (1983) 80:765. Chemokine-mediated histamine release from basophils is assayed as described in Dahinden et al., J. Exp. Med. (1989) 170:1787; and White et al., Immunol. Lett. (1989) 22:151. Heparin binding is described in Luster et al., J. Exp. Med. (1995) 182:219.

Chemokines can possess dimerization activity, which can be assayed according to Burrows et al., Biochem. (1994) 33:12741; and Zhang et al., Mol. Cell. Biol. (1995) 15:4851. Native chemokines can play a role in the inflammatory response of viruses. This activity can be assayed as described in Bleul et al., Nature (1996) 382:829; and Oberlin et al., Nature (1996) 382:833. Exocytosis of monocytes can be promoted by native chemokines. The assay for such activity is described in Uguccioni et al., Eur. J. Immunol. (1995) 25:64. Native chemokines also can inhibit hematopoietic stem cell proliferation. The method for testing for such activity is reported in Graham et al., Nature (1990) 344:442.

Death Domain Proteins. Several protein families contain death domain motifs

(Feinstein and Kimchi, *TIBS Letters* (1995) 20:242). Some death domain containing

proteins are implicated in cytotoxic intracellular signaling (Cleveland *et al.*, *Cell* (1995)

81:479, Pan *et al*, *Science* (1997) 276:111; Duan *et al.*, *Nature* (1997) 385:86-89, and

Chinnaiyan *et al*, *Science* (1996) 274:990). U.S. Patent No. 5,563,039 describes a protein

homologous to TRADD (Tumor Necrosis Factor Receptor-1 Associated Death Domain containing protein), and modifications of the active domain of TRADD that retain the functional characteristics of the protein, as well as apoptosis assays for testing the function of such death domain containing proteins. U.S. Patent No. 5,658,883 discloses biologically active TGF-B1 peptides. U.S. Patent No. 5,674,734 discloses RIP, which contains a C
terminal death domain and an N-terminal kinase domain.

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Leukemia Inhibitory Factor (LIF). An LIF profile is constructed from sequences of leukemia inhibitor factor, CT-1 (cardiotrophin-1), CNTF (ciliary neurotrophic factor), OSM (oncostatin M), and IL-6 (interleukin-6). This profile encompasses a family of secreted cytokines that have pleiotropic effects on many cell types including hepatocytes, osteoclasts, neuronal cells and cardiac myocytes, and can be used to detect additional genes encoding such proteins. These molecules are all structurally related and share a common co-receptor gp130 which mediates intracellular signal transduction by cytoplasmic tyrosine kinases such as src.

Novel proteins related to this family are also likely to be secreted, to activate gp130 and to function in the development of a variety of cell types. Thus new members of this family would be candidates to be developed as growth or survival factors for the cell types that they stimulate. For more details on this family of cytokines, see Pennica *et al*, *Cytokine and Growth Factor Reviews* (1996) 7:81-91. U.S. Patent No. 5,420,247 discloses LIF receptor and fusion proteins. U.S. Patent No. 5,443,825 discloses human LIF.

Angiopoietin. Angiopoietin-1 is a secreted ligand of the TIE-2 tyrosine kinase; it functions as an angiogenic factor critical for normal vascular development. Angiopoietin-2 is a natural antagonist of angiopoietin-1 and thus functions as an anti-angiogenic factor. These two proteins are structurally similar and activate the same receptor (Folkman *et al.*, *Cell* (1996) 87:1153, and Davis *et al.*, *Cell* (1996) 87:1161). The angiopoietin molecules are composed of two domains: a coiled-coil region and a region related to fibrinogen. The fibrinogen domain is found in many molecules including ficolin and tesascin, and is well defined structurally with many members.

<u>Receptor Protein-Tyrosine Kinases.</u> Receptor Protein-Tyrosine Kinases or RPTKs are described in Lindberg, *Annu. Rev. Cell Biol.* (1994) *10*:251-337.

Growth Factors: (Epidermal Growth Factor) EGF and (Fibroblast Growth Factor)

FGF. For a discussion of growth factor superfamilies, see *Growth Factors: A Practical Approach*, (Appendix A1) (1993) McKay and Leigh, Oxford University Press, NY, 237-243.

U.S. Patent No. 4,444,760 discloses acidic brain fibroblast growth factor, which is active in the promotion of cell division and wound healing. U.S. Patent No. 5,439,818 discloses DNA encoding human recombinant basic fibroblast growth factor, which is active in wound healing. U.S. Patent No. 5,604,293 discloses recombinant human basic fibroblast growth

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factor, which is useful for wound healing. U.S. Patent No. 5,410,832 discloses brain-derived and recombinant acidic fibroblast growth factor, which act as mitogens for mesoderm and neuroectoderm-derived cells in culture, and promote wound healing in soft tissue, cartilaginous tissue and musculo-skeletal tissue. U.S. Patent No. 5,387,673 discloses biologically active fragments of FGF.

Proteins of the TNF Family. A profile derived from the TNF family is created by aligning sequences of the following TNF family members: nerve growth factor (NGF), lymphotoxin, Fas ligand, tumor necrosis factor (TNFα), CD40 ligand, TRAIL, ox40 ligand, 4-1BB ligand, CD27 ligand, and CD30 ligand. The profile is designed to identify sequences of proteins that constitute new members or homologues of this family of proteins. U.S. Patent No. 5,606,023 discloses mutant TNF proteins; U.S. Patent No. 5,597,899 and U.S. Patent No. 5,486,463 disclose TNF muteins; and U.S. Patent No. 5,652,353 discloses DNA encoding TNFα muteins.

Members of the TNF family of proteins have been show in vitro to multimerize, as described in Burrows et al., Biochem. (1994) 33:12741 and Zhang et al., Mol. Cell. Biol. (1995) 15:4851 and bind receptors as described in Browning et al., J. Immunol. (1994) 147:1230, Androlewicz et al., J. Biol. Chem. (1992) 267:2542, and Crowe et al., Science (1994) 264:707.

In vivo, TNFs proteolytically cleave a target protein as described in Kriegel et al., 20 Cell (1988) 53:45 and Mohler et al., Nature (1994) 370:218 and demonstrate cell proliferation and differentiation activity. T-cell or thymocyte proliferation is assayed as described in Armitage et al., Eur. J. Immunol. (1992) 22:447; Current Protocols in Immunology, ed. J.E. Coligan et al., 3.1-3.19; Takai et al., J. Immunol. (1986) 137:3494-3500, Bertagnoli et al., J. Immunol. (1990) 145:1706, Bertagnoli et al., J. Immunol. (1991) 25 133:327, Bertagnoli et al., J. Immunol. (1992) 149:3778, and Bowman et al., J. Immunol. (1994) 152:1756. B cell proliferation and Ig secretion are assayed as described in Maliszewski, J. Immunol. (1990) 144:3028, and Assays for B Cell Function: In Vitro Antibody Production, Mond and Brunswick, Current Protocols in Immunol., Coligan Ed vol 1 pp 3.8.1-3.8.16, John Wiley and Sons, Toronto 1994, Kehrl et al., Science (1987) 238:1144 30 and Boussiotis et al., PNAS USA (1994) 91:7007. Other in vivo activities include upregulation of cell surface antigens, upregulation of costimulatory molecules, and cellular

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WO 99/33982 PCT/US98/27610 aggregation/adhesion as described in Barrett et al., J. Immunol. (1991) 146:1722; Bjorck et al., Eur. J. Immunol. (1993) 23:1771; Clark et al., Annu Rev. Immunol. (1991) 9:97; Ranheim et al., J. Exp. Med. (1994) 177:925; Yellin, J. Immunol. (1994) 153:666; and Gruss et al., Blood (1994) 84:2305.

Proliferation and differentiation of hematopoietic and lymphopoietic cells has also been shown in vivo for TNFs, using assays for embryonic differentiation and hematopoiesis as described in Johansson *et al.*, *Cellular Biology* (1995) *15*:141, Keller *et al.*, *Mol. Cell. Biol.* (1993) *13*:473, McClanahan *et al.*, *Blood* (1993) *81*:2903 and using assays to detect stem cell survival and differentiation as described in Culture of Hematopoietic Cells, Freshney *et al.* eds, pp 1-21, 23-29, 139-162, 163-179, and 265-268, Wiley-Liss, Inc., New York, NY, 1994, and Hirajama *et al.*, *PNAS USA* (1992) *89*:5907.

In vivo activities of TNFs also include lymphocyte survival and apoptosis, assayed as described in Darzynkewicz et al., Cytometry (1992) 13:795; Gorczca et al., Leukemia (1993) 7:659; Itoh et al., Cell (1991) 66:233; Zacharduk, J. Immunol. (1990) 145:4037; Zamai et al., Cytometry (1993) 14:891; and Gorczyca et al., Int'l J. Oncol. (1992) 1:639. Some members of the TNF family are cleaved from the cell surface; others remain membrane bound. The three-dimensional structure of TNF is discussed in Sprang and Eck, Tumor Necrosis Factors; supra.

TNF proteins include a transmembrane domain. The protein is cleaved into a shorter soluble version, as described in Kriegler *et al.*, *Cell* (1988) 53:45, Perez *et al.*, *Cell* (1990) 63:251, and Shaw *et al.*, *Cell* (1986) 46:659. The transmembrane domain is between amino acid 46 and 77 and the cytoplasmic domain is between position 1 and 45 on the human form of TNFα. The 3-dimensional motifs of TNF include a sandwich of two pleated β sheets. Each sheet is composed of anti-parallel β strands. β strands facing each other on opposite sites of the sandwich are connected by short polypeptide loops, as described in Van Ostade *et al.*, *Protein Engineering* (1994) 7(1):5, and Sprang *et al.*, Tumor Necrosis Factors; *supra*. Residues of the TNF family proteins that are involved in the β sheet secondary structure have been identified as described in Van Ostade *et al.*, *Protein Eng.* (1994) 7(1):5, and Sprang *et al.*, *supra*.

TNF receptors are disclosed in U.S. Patent No. 5,395,760. A profile derived from the TNF receptor family is created by aligning sequences of the TNF receptor family, including

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Apo1/Fas, TNFR I and II, death receptor 3 (DR3), CD40, ox40, CD27, and CD30. Thus, the profile is designed to identify from the polynucleotides of the invention sequences of proteins that constitute new members or homologues of this family of proteins.

Tumor necrosis factor receptors exist in two forms in humans: p55 TNFR and p75 TNFR, both of which provide intracellular signals upon binding with a ligand. The extracellular domains of these receptor proteins are cysteine rich. The receptors can remain membrane bound, although some forms of the receptors are cleaved forming soluble receptors. The regulation, diagnostic, prognostic, and therapeutic value of soluble TNF receptors is discussed in Aderka, *Cytokine and Growth Factor Reviews*, (1996) 7(3):231.

<u>PDGF Family.</u> U.S. Patent No. 5,326,695 discloses platelet derived growth factor agonists; bioactive portions of PDGF-B are used as agonists. U.S. Patent No. 4,845,075 discloses biologically active B-chain homodimers, and also includes variants and derivatives of the PDGF-B chain. U.S. Patent No. 5,128,321 discloses PDGF analogs and methods of use. Proteins having the same bioactivity as PDGF are disclosed, including A and B chain proteins.

<u>Kinase (Including MKK) Family.</u> U.S. Patent No. 5,650,501 discloses serine/threonine kinase, associated with mitotic and meiotic cell division; the protein has a kinase domain in its N-terminal and 3 PEST regions in the C-terminus. U.S. Patent No. 5,605,825 discloses human PAK65, a serine protein kinase.

The foregoing discussion provides a few examples of the protein profiles that can be compared with the polynucleotides of the invention. One skilled in the art can use these and other protein profiles to identify the genes that correlate with the provided polynucleotides.

C. <u>Identification of Secreted & Membrane-Bound Polypeptides</u>

Both secreted and membrane-bound polypeptides of the present invention are of particular interest. For example, levels of secreted polypeptides can be assayed in body fluids that are convenient, such as blood, urine, prostatic fluid and semen. Membrane-bound polypeptides are useful for constructing vaccine antigens or inducing an immune response. Such antigens would comprise all or part of the extracellular region of the membrane-bound polypeptides. Because both secreted and membrane-bound polypeptides comprise a fragment of contiguous hydrophobic amino acids, hydrophobicity predicting algorithms can be used to identify such polypeptides.

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A signal sequence is usually encoded by both secreted and membrane-bound polypeptide genes to direct a polypeptide to the surface of the cell. The signal sequence usually comprises a stretch of hydrophobic residues. Such signal sequences can fold into helical structures. Membrane-bound polypeptides typically comprise at least one transmembrane region that possesses a stretch of hydrophobic amino acids that can transverse the membrane. Some transmembrane regions also exhibit a helical structure. Hydrophobic fragments within a polypeptide can be identified by using computer algorithms. Such algorithms include Hopp & Woods, *Proc. Natl. Acad. Sci. USA* (1981) 78:3824-3828; Kyte & Doolittle, *J. Mol. Biol.* (1982) 157: 105-132; and RAOAR algorithm, Degli Esposti *et al.*, *Eur. J. Biochem.* (1990) 190: 207-219.

Another method of identifying secreted and membrane-bound polypeptides is to translate the polynucleotides of the invention in all six frames and determine if at least 8 contiguous hydrophobic amino acids are present. Those translated polypeptides with at least 8; more typically, 10; even more typically, 12 contiguous hydrophobic amino acids are considered to be either a putative secreted or membrane bound polypeptide. Hydrophobic amino acids include alanine, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, threonine, tryptophan, tyrosine, and valine.

IV. <u>Identification of the Function of an Expression Product of a Full-Length Gene</u> <u>Corresponding to a Polynucleotide</u>

Ribozymes, antisense constructs, and dominant negative mutants can be used to determine function of the expression product of a gene corresponding to a polynucleotide provided herein. These methods and compositions are particularly useful where the provided novel polynucleotide exhibits no significant or substantial homology to a sequence encoding a gene of known function. Antisense molecules and ribozymes can be constructed from synthetic polynucleotides. Typically, the phosphoramidite method of oligonucleotide synthesis is used. See Beaucage *et al.*, *Tet. Lett.* (1981) 22:1859 and U.S. Patent No. 4,668,777. Automated devices for synthesis are available to create oligonucleotides using this chemistry. Examples of such devices include Biosearch 8600, Models 392 and 394 by Applied Biosystems, a division of Perkin-Elmer Corp., Foster City, California, USA; and Expedite by Perceptive Biosystems, Framingham, Massachusetts, USA. Synthetic RNA,

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phosphate analog oligonucleotides, and chemically derivatized oligonucleotides can also be produced, and can be covalently attached to other molecules. RNA oligonucleotides can be synthesized, for example, using RNA phosphoramidites. This method can be performed on an automated synthesizer, such as Applied Biosystems, Models 392 and 394, Foster City, California, USA. See Applied Biosystems User Bulletin 53 and Ogilvie *et al.*, *Pure & Applied Chem.* (1987) 59:325.

Phosphorothioate oligonucleotides can also be synthesized for antisense construction. A sulfurizing reagent, such as tetraethylthiruam disulfide (TETD) in acetonitrile can be used to convert the internucleotide cyanoethyl phosphite to the phosphorothioate triester within 15 minutes at room temperature. TETD replaces the iodine reagent, while all other reagents used for standard phosphoramidite chemistry remain the same. Such a synthesis method can be automated using Models 392 and 394 by Applied Biosystems, for example.

Oligonucleotides of up to 200 nucleotides can be synthesized, more typically, 100 nucleotides, more typically 50 nucleotides; even more typically 30 to 40 nucleotides. These synthetic fragments can be annealed and ligated together to construct larger fragments. See, for example, Sambrook *et al.*, *supra*.

A. Ribozymes

Trans-cleaving catalytic RNAs (ribozymes) are RNA molecules possessing endoribonuclease activity. Ribozymes are specifically designed for a particular target, and the target message must contain a specific nucleotide sequence. They are engineered to cleave any RNA species site-specifically in the background of cellular RNA. The cleavage event renders the mRNA unstable and prevents protein expression. Importantly, ribozymes can be used to inhibit expression of a gene of unknown function for the purpose of determining its function in an in vitro or in vivo context, by detecting the phenotypic effect.

One commonly used ribozyme motif is the hammerhead, for which the substrate sequence requirements are minimal. Design of the hammerhead ribozyme is disclosed in Usman *et al.*, *Current Opin. Struct. Biol.* (1996) 6:527. Usman also discusses the therapeutic uses of ribozymes. Ribozymes can also be prepared and used as described in Long *et al.*, *FASEB J.* (1993) 7:25; Symons, *Ann. Rev. Biochem.* (1992) 61:641; Perrotta *et al.*, *Biochem.* (1992) 31:16; Ojwang *et al.*, *Proc. Natl. Acad. Sci. (USA)* (1992) 89:10802; and U.S. Patent No. 5,254,678. Ribozyme cleavage of HIV-I RNA is described in U.S.

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Patent No. 5,144,019; methods of cleaving RNA using ribozymes is described in U.S. Patent No. 5,116,742; and methods for increasing the specificity of ribozymes are described in U.S. Patent No. 5,225,337 and Koizumi *et al.*, *Nucleic Acid Res.* (1989) 17:7059. Preparation and use of ribozyme fragments in a hammerhead structure are also described by Koizumi *et al.*, *Nucleic Acids Res.* (1989) 17:7059. Preparation and use of ribozyme fragments in a hairpin structure are described by Chowrira and Burke, *Nucleic Acids Res.* (1992) 20:2835. Ribozymes can also be made by rolling transcription as described in Daubendiek and Kool, *Nat. Biotechnol.* (1997) 15(3):273.

The hybridizing region of the ribozyme can be modified or can be prepared as a branched structure as described in Horn and Urdea, *Nucleic Acids Res.* (1989) 17:6959. The basic structure of the ribozymes can also be chemically altered in ways familiar to those skilled in the art, and chemically synthesized ribozymes can be administered as synthetic oligonucleotide derivatives modified by monomeric units. In a therapeutic context, liposome mediated delivery of ribozymes improves cellular uptake, as described in Birikh *et al.*, *Eur. J. Biochem.* (1997) 245:1.

Using the polynucleotide sequences of the invention and methods known in the art, ribozymes are designed to specifically bind and cut the corresponding mRNA species. Ribozymes thus provide a means to inhibit the expression of any of the proteins encoded by the disclosed polynucleotides or their full-length genes. The full-length gene need not be known in order to design and use specific inhibitory ribozymes. In the case of a polynucleotide or full-length cDNA of unknown function, ribozymes corresponding to that nucleotide sequence can be tested in vitro for efficacy in cleaving the target transcript. Those ribozymes that effect cleavage in vitro are further tested in vivo. The ribozyme can also be used to generate an animal model for a disease, as described in Birikh *et al.*, *supra*. An effective ribozyme is used to determine the function of the gene of interest by blocking its transcription and detecting a change in the cell. Where the gene is found to be a mediator in a disease, an effective ribozyme is designed and delivered in a gene therapy for blocking transcription and expression of the gene.

Therapeutic and functional genomic applications of ribozymes proceed beginning with knowledge of a portion of the coding sequence of the gene to be inhibited. Thus, for many genes, a partial polynucleotide sequence provides adequate sequence for constructing

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an effective ribozyme. A target cleavage site is selected in the target sequence, and a ribozyme is constructed based on the 5' and 3' nucleotide sequences that flank the cleavage site. Retroviral vectors are engineered to express monomeric and multimeric hammerhead ribozymes targeting the mRNA of the target coding sequence. These monomeric and multimeric ribozymes are tested in vitro for an ability to cleave the target mRNA. A cell line is stably transduced with the retroviral vectors expressing the ribozymes, and the transduction is confirmed by Northern blot analysis and reverse-transcription polymerase chain reaction (RT-PCR). The cells are screened for inactivation of the target mRNA by such indicators as reduction of expression of disease markers or reduction of the gene product of the target mRNA.

B. Antisense

Antisense nucleic acids are designed to specifically bind to RNA, resulting in the formation of RNA-DNA or RNA-RNA hybrids, with an arrest of DNA replication, reverse transcription or messenger RNA translation. Antisense polynucleotides based on a selected polynucleotide sequence can interfere with expression of the corresponding gene. Antisense polynucleotides are typically generated within the cell by expression from antisense constructs that contain the antisense strand as the transcribed strand. Antisense polynucleotides based on the disclosed polynucleotides will bind and/or interfere with the translation of mRNA comprising a sequence complementary to the antisense polynucleotide. The expression products of control cells and cells treated with the antisense construct are compared to detect the protein product of the gene corresponding to the polynucleotide upon which the antisense construct is based. The protein is isolated and identified using routine biochemical methods.

One rationale for using antisense methods to determine the function of the gene corresponding to a disclosed polynucleotide is the biological activity of antisense therapeutics. Antisense therapy for a variety of cancers is in clinical phase and has been discussed extensively in the literature. Reed reviewed antisense therapy directed at the Bcl-2 gene in tumors; gene transfer-mediated overexpression of Bcl-2 in tumor cell lines conferred resistance to many types of cancer drugs. (Reed, J.C., N.C.I. (1997) 89:988). The potential for clinical development of antisense inhibitors of ras is discussed by Cowsert, L.M., Anti-Cancer Drug Design (1997) 12:359. Additional important antisense targets include

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WO 99/33982 PCT/US98/27610 leukemia (Geurtz, A.M., Anti-Cancer Drug Design (1997) 12:341); human C-ref kinase (Monia, B.P., Anti-Cancer Drug Design (1997) 12:327); and protein kinase C (McGraw et al., Anti-Cancer Drug Design (1997) 12:315.

Given the extensive background literature and clinical experience in antisense therapy, one skilled in the art can use selected polynucleotides of the invention as additional potential therapeutics. The choice of polynucleotide can be narrowed by first testing them for binding to "hot spot" regions of the genome of cancerous cells. If a polynucleotide is identified as binding to a "hot spot", testing the polynucleotide as an antisense compound in the corresponding cancer cells clearly is warranted.

Ogunbiyi et al., Gastroenterology (1997) 113(3):761 describe prognostic use of allelic loss in colon cancer; Barks et al., Genes, Chromosomes, and Cancer (1997) 19(4):278 describe increased chromosome copy number detected by FISH in malignant melanoma; Nishizake et al., Genes, Chromosomes, and Cancer (1997) 19(4):267 describe genetic alterations in primary breast cancer and their metastases and direct comparison using modified comparative genome hybridization; and Elo et al., Cancer Research (1997) 57(16):3356 disclose that loss of heterozygosity at 16z24.1-q24.2 is significantly associated with metastatic and aggressive behavior of prostate cancer.

C. Dominant Negative Mutations

As an alternative method for identifying function of the gene corresponding to a

20 polynucleotide disclosed herein, dominant negative mutations are readily generated for
corresponding proteins that are active as homomultimers. A mutant polypeptide will interact
with wild-type polypeptides (made from the other allele) and form a non-functional
multimer. Thus, a mutation is in a substrate-binding domain, a catalytic domain, or a
cellular localization domain. Preferably, the mutant polypeptide will be overproduced.

Point mutations are made that have such an effect. In addition, fusion of different polypeptides of various lengths to the terminus of a protein can yield dominant negative mutants. General strategies are available for making dominant negative mutants (see, e.g., Herskowitz, *Nature* (1987) 329:219). Such techniques can be used to create loss of function mutations, which are useful for determining protein function.

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V. Construction of Polypeptides of the Invention and Variants Thereof

The polypeptides of the invention include those encoded by the disclosed polynucleotides. These polypeptides can also be encoded by nucleic acids that, by virtue of the degeneracy of the genetic code, are not identical in sequence to the disclosed polynucleotides. Thus, the invention includes within its scope a polypeptide encoded by a polynucleotide having the sequence of any one of SEQ ID NOS: 1-844 or a variant thereof.

In general, the term "polypeptide" as used herein refers to both the full length polypeptide encoded by the recited polynucleotide, the polypeptide encoded by the gene represented by the recited polynucleotide, as well as portions or fragments thereof.
"Polypeptides" also includes variants of the naturally occurring proteins, where such variants are homologous or substantially similar to the naturally occurring protein, and can be of an origin of the same or different species as the naturally occurring protein (*e.g.*, human, murine, or some other species that naturally expresses the recited polypeptide, usually a mammalian species). In general, variant polypeptides have a sequence that has at least about 80%, usually at least about 90%, and more usually at least about 98% sequence identity with a differentially expressed polypeptide of the invention, as measured by BLAST using the parameters described above. The variant polypeptides can be naturally or non-naturally glycosylated, *i.e.*, the polypeptide has a glycosylation pattern that differs from the glycosylation pattern found in the corresponding naturally occurring protein.

The invention also encompasses homologs of the disclosed polypeptides (or fragments thereof) where the homologs are isolated from other species, *i.e.* other animal or plant species, where such homologs, usually mammalian species, *e.g.* rodents, such as mice, rats; domestic animals, *e.g.*, horse, cow, dog, cat; and humans. By homolog is meant a polypeptide having at least about 35%, usually at least about 40% and more usually at least about 60% amino acid sequence identity a particular differentially expressed protein as identified above, where sequence identity is determined using the BLAST algorithm, with the parameters described *supra*.

In general, the polypeptides of the subject invention are provided in a non-naturally occurring environment, *e.g.* are separated from their naturally occurring environment. In certain embodiments, the subject protein is present in a composition that is enriched for the protein as compared to a control. As such, purified polypeptide is provided, where by

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purified is meant that the protein is present in a composition that is substantially free of non-differentially expressed polypeptides, where by substantially free is meant that less than 90%, usually less than 60% and more usually less than 50% of the composition is made up of non-differentially expressed polypeptides.

Also within the scope of the invention are variants; variants of polypeptides include mutants, fragments, and fusions. Mutants can include amino acid substitutions, additions or deletions. The amino acid substitutions can be conservative amino acid substitutions or substitutions to eliminate non-essential amino acids, such as to alter a glycosylation site, a phosphorylation site or an acetylation site, or to minimize misfolding by substitution or deletion of one or more cysteine residues that are not necessary for function. Conservative amino acid substitutions are those that preserve the general charge, hydrophobicity/hydrophilicity, and/or steric bulk of the amino acid substituted. For example, substitutions between the following groups are conservative: Gly/Ala, Val/Ile/Leu, Asp/Glu, Lys/Arg, Asn/Gln, Ser/Cys, Thr, and Phe/Trp/Tyr.

Variants can be designed so as to retain biological activity of a particular region of the protein (e.g., a functional domain and/or, where the polypeptide is a member of a protein family, a region associated with a consensus sequence). In a non-limiting example, Osawa et al., Biochem. Mol. Int. (1994) 34:1003, discusses the actin binding region of a protein from several different species. The actin binding regions of the these species are considered homologous based on the fact that they have amino acids that fall within "homologous residue groups." Homologous residues are judged according to the following groups (using single letter amino acid designations): STAG; ILVMF; HRK; DEQN; and FYW. For example, and S, a T, an A or a G can be in a position and the function (in this case actin binding) is retained.

Additional guidance on amino acid substitution is available from studies of protein evolution. Go *et al*, *Int. J. Peptide Protein Res.* (1980) *15*:211, classified amino acid residue sites as interior or exterior depending on their accessibility. More frequent substitution on exterior sites was confirmed to be general in eight sets of homologous protein families regardless of their biological functions and the presence or absence of a prosthetic group. Virtually all types of amino acid residues had higher mutabilities on the exterior than in the interior. No correlation between mutability and polarity was observed of amino acid

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wo 99/33982 PCT/US98/27610 residues in the interior and exterior, respectively. Amino acid residues were classified into one of three groups depending on their polarity: polar (Arg, Lys, His, Gln, Asn, Asp, and Glu); weak polar (Ala, Pro, Gly, Thr, and Ser), and nonpolar (Cys, Val, Met, Ile, Leu, Phe, Tyr, and Trp). Amino acid replacements during protein evolution were very conservative: 88% and 76% of them in the interior or exterior, respectively, were within the same group of the three. Inter-group replacements are such that weak polar residues are replaced more often by nonpolar residues in the interior and more often by polar residues on the exterior.

Additional guidance for production of polypeptide variants is provided in Querol et al., Prot. Eng. (1996) 9:265, which provides general rules for amino acid substitutions to enhance protein thermostability. New glycosylation sites can be introduced as discussed in Olsen and Thomsen, J. Gen. Microbiol. (1991) 137:579. An additional disulfide bridge can be introduced, as discussed by Perry and Wetzel, Science (1984) 226:555; Pantoliano et al., Biochemistry (1987) 26:2077; Matsumura et al., Nature (1989) 342:291; Nishikawa et al., Protein Eng. (1990) 3:443; Takagi et al., J. Biol. Chem. (1990) 265:6874; Clarke et al., Biochemistry (1993) 32:4322; and Wakarchuk et al., Protein Eng. (1994) 7:1379. Metal binding sites can be introduced, according to Toma et al., Biochemistry (1991) 30:97, and Haezerbrouck et al., Protein Eng. (1993) 6:643. Substitutions with prolines in loops can be made according to Masul et al., Appl. Env. Microbiol. (1994) 60:3579; and Hardy et al., FEBS Lett. 317:89.

Cysteine-depleted muteins are considered variants within the scope of the invention. These variants can be constructed according to methods disclosed in U.S. Patent No. 4,959,314, which discloses substitution of cysteines with other amino acids, and methods for assaying biological activity and effect of the substitution. Such methods are suitable for proteins according to this invention that have cysteine residues suitable for such substitutions, for example to eliminate disulfide bond formation.

Variants also include fragments of the polypeptides disclosed herein, particularly biologically active fragments and/or fragments corresponding to functional domains. Fragments of interest will typically be at least about 10 aa to at least about 15 aa in length, usually at least about 50 aa in length, and can be as long as 300 aa in length or longer, but will usually not exceed about 1000 aa in length, where the fragment will have a stretch of

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amino acids that is identical to a polypeptide encoded by a polynucleotide having a sequence of any SEQ ID NOS:1-844, or a homolog thereof.

The protein variants described herein are encoded by polynucleotides that are within the scope of the invention. The genetic code can be used to select the appropriate codons to construct the corresponding variants.

VI. Computer-Related Embodiments

In general, a library of polynucleotides is a collection of sequence information, which information is provided in either biochemical form (*e.g.*, as a collection of polynucleotide molecules), or in electronic form (*e.g.*, as a collection of polynucleotide sequences stored in a computer-readable form, as in a computer system and/or as part of a computer program). The sequence information of the polynucleotides can be used in a variety of ways, *e.g.*, as a resource for gene discovery, as a representation of sequences expressed in a selected cell type (*e.g.*, cell type markers), and/or as markers of a given disease or disease state. In general, a disease marker is a representation of a gene product that is present in all affected by disease either at an increased or decreased level relative to a normal cell (*e.g.*, a cell of the same or similar type that is not substantially affected by disease). For example, a polynucleotide sequence in a library can be a polynucleotide that represents an mRNA, polypeptide, or other gene product encoded by the polynucleotide, that is either overexpressed or underexpressed in a breast ductal cell affected by cancer relative to a normal (*i.e.*, substantially disease-free) breast cell.

The nucleotide sequence information of the library can be embodied in any suitable form, *e.g.*, electronic or biochemical forms. For example, a library of sequence information embodied in electronic form includes an accessible computer data file (or, in biochemical form, a collection of nucleic acid molecules) that contains the representative nucleotide sequences of genes that are differentially expressed (*e.g.*, overexpressed or underexpressed) as between, for example, i) a cancerous cell and a normal cell; ii) a cancerous cell and a dysplastic cell; iii) a cancerous cell and a cell affected by a disease or condition other than cancer; iv) a metastatic cancerous cell and a normal cell and/or non-metastatic cancerous cell; v) a malignant cancerous cell and a non-malignant cancerous cell (or a normal cell) and/or vi) a dysplastic cell relative to a normal cell. Other combinations and comparisons of

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cells affected by various diseases or stages of disease will be readily apparent to the ordinarily skilled artisan. Biochemical embodiments of the library include a collection of nucleic acids that have the sequences of the genes in the library, where the nucleic acids can correspond to the entire gene in the library or to a fragment thereof, as described in greater detail below.

The polynucleotide libraries of the subject invention include sequence information of a plurality of polynucleotide sequences, where at least one of the polynucleotides has a sequence of any of SEQ ID NOS:1-844. By plurality is meant at least 2, usually at least 3 and can include up to all of SEQ ID NOS:1-844. The length and number of polynucleotides in the library will vary with the nature of the library, *e.g.*, if the library is an oligonucleotide array, a cDNA array, a computer database of the sequence information, etc.

Where the library is an electronic library, the nucleic acid sequence information can be present in a variety of media. "Media" refers to a manufacture, other than an isolated nucleic acid molecule, that contains the sequence information of the present invention. Such a manufacture provides the genome sequence or a subset thereof in a form that can be examined by means not directly applicable to the sequence as it exists in a nucleic acid. For example, the nucleotide sequence of the present invention, e.g. the nucleic acid sequences of any of the polynucleotides of SEQ ID NOS:1-844, can be recorded on computer readable media, e.g. any medium that can be read and accessed directly by a computer. Such media include, but are not limited to: magnetic storage media, such as a floppy disc, a hard disc storage medium, and a magnetic tape; optical storage media such as CD-ROM; electrical storage media such as RAM and ROM; and hybrids of these categories such as magnetic/optical storage media. One of skill in the art can readily appreciate how any of the presently known computer readable mediums can be used to create a manufacture comprising a recording of the present sequence information. "Recorded" refers to a process for storing information on computer readable medium, using any such methods as known in the art. Any convenient data storage structure can be chosen, based on the means used to access the stored information. A variety of data processor programs and formats can be used for storage, e.g. word processing text file, database format, etc. In addition to the sequence information, electronic versions of the libraries of the invention can be provided in conjunction or connection with other computer-readable information and/or other types of

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WO 99/33982 PCT/US98/27610 computer-readable files (*e.g.*, searchable files, executable files, *etc*, including, but not limited to, for example, search program software, *etc.*.).

By providing the nucleotide sequence in computer readable form, the information can be accessed for a variety of purposes. Computer software to access sequence information is publicly available. For example, the BLAST (Altschul *et al.*, *supra.*) and BLAZE (Brutlag *et al. Comp. Chem.* (1993) 17:203) search algorithms on a Sybase system can be used identify open reading frames (ORFs) within the genome that contain homology to ORFs from other organisms.

As used herein, "a computer-based system" refers to the hardware means, software means, and data storage means used to analyze the nucleotide sequence information of the present invention. The minimum hardware of the computer-based systems of the present invention comprises a central processing unit (CPU), input means, output means, and data storage means. A skilled artisan can readily appreciate that any one of the currently available computer-based system are suitable for use in the present invention. The data storage means can comprise any manufacture comprising a recording of the present sequence information as described above, or a memory access means that can access such a manufacture.

"Search means" refers to one or more programs implemented on the computer-based system, to compare a target sequence or target structural motif with the stored sequence information. Search means are used to identify fragments or regions of the genome that match a particular target sequence or target motif. A variety of known algorithms are publicly known and commercially available, *e.g.* MacPattern (EMBL), BLASTN and BLASTX (NCBI). A "target sequence" can be any DNA or amino acid sequence of six or more nucleotides or two or more amino acids, preferably from about 10 to 100 amino acids or from about 30 to 300 nucleotide residues.

A "target structural motif," or "target motif," refers to any rationally selected sequence or combination of sequences in which the sequence(s) are chosen based on a three-dimensional configuration that is formed upon the folding of the target motif, or on consensus sequences of regulatory or active sites. There are a variety of target motifs known in the art. Protein target motifs include, but are not limited to, enzyme active sites and signal sequences. Nucleic acid target motifs include, but are not limited to, hairpin structures,

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promoter sequences and other expression elements such as binding sites for transcription factors.

A variety of structural formats for the input and output means can be used to input and output the information in the computer-based systems of the present invention. One format for an output means ranks fragments of the genome possessing varying degrees of homology to a target sequence or target motif. Such presentation provides a skilled artisan with a ranking of sequences and identifies the degree of sequence similarity contained in the identified fragment.

A variety of comparing means can be used to compare a target sequence or target motif with the data storage means to identify sequence fragments of the genome. A skilled artisan can readily recognize that any one of the publicly available homology search programs can be used as the search means for the computer based systems of the present invention.

As discussed above, the "library" of the invention also encompasses biochemical libraries of the polynucleotides of SEQ ID NOS:1-844, e.g., collections of nucleic acids representing the provided polynucleotides. The biochemical libraries can take a variety of forms, e.g., a solution of cDNAs, a pattern of probe nucleic acids stably associated with a surface of a solid support (i.e., an array) and the like. Of particular interest are nucleic acid arrays in which one or more of SEQ ID NOS:1-844 is represented on the array. By array is meant a an article of manufacture that has at least a substrate with at least two distinct nucleic acid targets on one of its surfaces, where the number of distinct nucleic acids can be considerably higher, typically being at least 10 nt, usually at least 20 nt and often at least 25 nt. A variety of different array formats have been developed and are known to those of skill in the art, including those described in 5,242,974; 5,384,261; 5,405,783; 5,412,087; 5,424,186; 5,429,807; 5,436,327; 5,445,934; 5,472,672; 5,527,681; 5,529,756; 5,545,531; 5,554,501; 5,556,752; 5,561,071; 5,599,895; 5,624,711; 5,639,603; 5,658,734; WO 93/17126; WO 95/11995; WO 95/35505; EP 742287; and EP 799897. The arrays of the subject invention find use in a variety of applications, including gene expression analysis, drug screening, mutation analysis and the like, as disclosed in the above-listed exemplary patent documents.

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In addition to the above nucleic acid libraries, analogous libraries of polypeptides are also provided, where the where the polypeptides of the library will represent at least a portion of the polypeptides encoded by SEQ ID NOS:1-844.

5 VII. Utilities

A. <u>Use of Polynucleotide Probes in Mapping, and in Tissue Profiling</u>

Polynucleotide probes, generally comprising at least 12 contiguous nucleotides of a polynucleotide as shown in the Sequence Listing, are used for a variety of purposes, such as chromosome mapping of the polynucleotide and detection of transcription levels. Additional disclosure about preferred regions of the disclosed polynucleotide sequences is found in the Examples. A probe that hybridizes specifically to a polynucleotide disclosed herein should provide a detection signal at least 5-, 10-, or 20-fold higher than the background hybridization provided with other unrelated sequences.

Probes in Detection of Expression Levels. Nucleotide probes are used to detect expression of a gene corresponding to the provided polynucleotide. The references describe an example of a sandwich nucleotide hybridization assay. For example, in Northern blots, mRNA is separated electrophoretically and contacted with a probe. A probe is detected as hybridizing to an mRNA species of a particular size. The amount of hybridization is quantitated to determine relative amounts of expression, for example under a particular condition. Probes are also used to detect products of amplification by polymerase chain reaction. The products of the reaction are hybridized to the probe and hybrids are detected. Probes are used for in situ hybridization to cells to detect expression. Probes can also be used *in vivo* for diagnostic detection of hybridizing sequences. Probes are typically labeled with a radioactive isotope. Other types of detectable labels can be used such as chromophores, fluors, and enzymes. Other examples of nucleotide hybridization assays are described in WO92/02526 and U.S. Patent No. 5,124,246.

Alternatively, the Polymerase Chain Reaction (PCR) is another means for detecting small amounts of target nucleic acids (see, *e.g.*, Mullis *et al.*, *Meth. Enzymol.* (1987) *155*:335; U.S. Patent No. 4,683,195; and U.S. Patent No. 4,683,202). Two primer polynucleotides nucleotides hybridize with the target nucleic acids and are used to prime the reaction. The primers can be composed of sequence within or 3' and 5' to the polynucleotides of the Sequence Listing. Alternatively, if the primers are 3' and 5' to these

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polynucleotides, they need not hybridize to them or the complements. A thermostable polymerase creates copies of target nucleic acids from the primers using the original target nucleic acids as a template. After a large amount of target nucleic acids is generated by the polymerase, it is detected by methods such as Southern blots. When using the Southern blot method, the labeled probe will hybridize to a polynucleotide of the Sequence Listing or complement.

Furthermore, mRNA or cDNA can be detected by traditional blotting techniques described in Sambrook *et al.*, "Molecular Cloning: A Laboratory Manual" (New York, Cold Spring Harbor Laboratory, 1989). mRNA or cDNA generated from mRNA using a polymerase enzyme can be purified and separated using gel electrophoresis. The nucleic acids on the gel are then blotted onto a solid support, such as nitrocellulose. The solid support is exposed to a labeled probe and then washed to remove any unhybridized probe. Next, the duplexes containing the labeled probe are detected. Typically, the probe is labeled with radioactivity.

Mapping. Polynucleotides of the present invention are used to identify a chromosome on which the corresponding gene resides. Such mapping can be useful in identifying the function of the polynucleotide-related gene by its proximity to other genes with known function. Function can also be assigned to the polynucleotide-related gene when particular syndromes or diseases map to the same chromosome. For example, use of polynucleotide probes in identification and quantification of nucleic acid sequence aberrations is described in U.S. Patent No. 5,783,387.

For example, fluorescence in situ hybridization (FISH) on normal metaphase spreads facilitates comparative genomic hybridization to allow total genome assessment of changes in relative copy number of DNA sequences. See Schwartz and Samad, *Curr. Opin.*25 *Biotechnol.* (1994) 8:70; Kallioniemi *et al.*, *Sem. Cancer Biol.* (1993) 4:41; Valdes *et al.*, *Methods in Molecular Biology* (1997) 68:1, Boultwood, ed., Human Press, Totowa, NJ. Preparations of human metaphase chromosomes are prepared using standard cytogenetic techniques from human primary tissues or cell lines. Nucleotide probes comprising at least 12 contiguous nucleotides selected from the nucleotide sequence shown in the Sequence

Listing are used to identify the corresponding chromosome. The nucleotide probes are labeled, for example, with a radioactive, fluorescent, biotinylated, or chemiluminescent label,

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WO 99/33982 PCT/US98/27610 and detected by well known methods appropriate for the particular label selected. Protocols for hybridizing nucleotide probes to preparations of metaphase chromosomes are also well known in the art. A nucleotide probe will hybridize specifically to nucleotide sequences in the chromosome preparations that are complementary to the nucleotide sequence of the probe.

Polynucleotides are mapped to particular chromosomes using, for example, radiation hybrids or chromosome-specific hybrid panels. See Leach *et al.*, *Advances in Genetics*, (1995) *33*:63-99; Walter *et al.*, *Nature Genetics* (1994) 7:22; Walter and Goodfellow, *Trends in Genetics* (1992) 9:352. Panels for radiation hybrid mapping are available from Research Genetics, Inc., Huntsville, Alabama, USA. Databases for markers using various panels are available via the world wide web at http://F/shgc-www.stanford.edu; and http://www-genome.wi.mit.edu/cgi-bin/contig/rhmapper.pl. The statistical program RHMAP can be used to construct a map based on the data from radiation hybridization with a measure of the relative likelihood of one order versus another. RHMAP is available via the world wide web at http://www.sph.umich.edu/group/statgen/software.

In addition, commercial programs are available for identifying regions of chromosomes commonly associated with disease, such as cancer. Polynucleotides based on the polynucleotides of the invention can be used to probe these regions. For example, if through profile searching a provided polynucleotide is identified as corresponding to a gene encoding a kinase, its ability to bind to a cancer-related chromosomal region will suggest its role as a kinase in one or more stages of tumor cell development/growth. Although some experimentation would be required to elucidate the role, the polynucleotide constitutes a new material for isolating a specific protein that has potential for developing a cancer diagnostic or therapeutic.

<u>Tissue Typing or Profiling.</u> Expression of specific mRNA corresponding to the provided polynucleotides can vary in different cell types and can be tissue-specific. This variation of mRNA levels in different cell types can be exploited with nucleic acid probe assays to determine tissue types. For example, PCR, branched DNA probe assays, or blotting techniques utilizing nucleic acid probes substantially identical or complementary to polynucleotides listed in the Sequence Listing can determine the presence or absence of the corresponding cDNA or mRNA.

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For example, a metastatic lesion is identified by its developmental organ or tissue

source by identifying the expression of a particular marker of that organ or tissue. If a polynucleotide is expressed only in a specific tissue type, and a metastatic lesion is found to express that polynucleotide, then the developmental source of the lesion has been identified. Expression of a particular polynucleotide is assayed by detection of either the corresponding mRNA or the protein product. Immunological methods, such as antibody staining, are used to detect a particular protein product. Hybridization methods can be used to detect particular

mRNA species, including but not limited to in situ hybridization and Northern blotting.

Use of Polymorphisms. A polynucleotide of the invention will be useful in forensics, genetic analysis, mapping, and diagnostic applications if the corresponding region of a gene is polymorphic in the human population. Particular polymorphic forms of the provided polynucleotides can be used to either identify a sample as deriving from a suspect or rule out the possibility that the sample derives from the suspect. Any means for detecting a polymorphism in a gene are used, including but not limited to electrophoresis of protein polymorphic variants, differential sensitivity to restriction enzyme cleavage, and hybridization to allele-specific probes.

B. Antibody Production

Expression products of a polynucleotide of the invention, the corresponding mRNA or cDNA, or the corresponding complete gene are prepared and used for raising antibodies for experimental, diagnostic, and therapeutic purposes. For polynucleotides to which a corresponding gene has not been assigned, this provides an additional method of identifying the corresponding gene. The polynucleotide or related cDNA is expressed as described above, and antibodies are prepared. These antibodies are specific to an epitope on the polypeptide encoded by the polynucleotide, and can precipitate or bind to the corresponding native protein in a cell or tissue preparation or in a cell-free extract of an in vitro expression system.

Immunogens for raising antibodies are prepared by mixing the polypeptides encoded by the polynucleotides of the present invention with adjuvants. Alternatively, polypeptides are made as fusion proteins to larger immunogenic proteins. Polypeptides are also covalently linked to other larger immunogenic proteins, such as keyhole limpet hemocyanin. Immunogens are typically administered intradermally, subcutaneously, or intramuscularly.

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Immunogens are administered to experimental animals such as rabbits, sheep, and mice, to generate antibodies. Optionally, the animal spleen cells are isolated and fused with myeloma cells to form hybridomas which secrete monoclonal antibodies. Such methods are well known in the art. According to another method known in the art, the selected polynucleotide is administered directly, such as by intramuscular injection, and expressed in vivo. The expressed protein generates a variety of protein-specific immune responses, including production of antibodies, comparable to administration of the protein.

Preparations of polyclonal and monoclonal antibodies specific for polypeptides encoded by a selected polynucleotide are made using standard methods known in the art. The antibodies specifically bind to epitopes present in the polypeptides encoded by polynucleotides disclosed in the Sequence Listing. Typically, at least 6, 8, 10, or 12 contiguous amino acids are required to form an epitope. However, epitopes which involve non-contiguous amino acids may require more, for example at least 15, 25, or 50 amino acids. A short sequence of a polynucleotide may then be unsuitable for use as an epitope to raise antibodies for identifying the corresponding novel protein, because of the potential for cross-reactivity with a known protein. However, the antibodies can be useful for other purposes, particularly if they identify common structural features of a known protein and a novel polypeptide encoded by a polynucleotide of the invention.

Antibodies that specifically bind to human polypeptides encoded by the provided polypeptides should provide a detection signal at least 5-, 10-, or 20-fold higher than a detection signal provided with other proteins when used in Western blots or other immunochemical assays. Preferably, antibodies that specifically polypeptides of the invention do not bind to other proteins in immunochemical assays at detectable levels and can immunoprecipitate the specific polypeptide from solution.

To test for the presence of serum antibodies to the polypeptide of the invention in a human population, human antibodies are purified by methods well known in the art.

Preferably, the antibodies are affinity purified by passing antiserum over a column to which the corresponding selected polypeptide or fusion protein is bound. The bound antibodies can then be eluted from the column, for example using a buffer with a high salt concentration.

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In addition to the antibodies discussed above, genetically engineered antibody derivatives are made, such as single chain antibodies, according to methods well known in the art.

C. <u>Use of Polynucleotides to Construct Arrays for Diagnostics</u>

Polynucleotide arrays provide a high throughput technique that can assay a large number of polynucleotide sequences in a sample. This technology can be used as a diagnostic and as a tool to test for differential expression to determine function of an encoded protein. Arrays can be created by spotting polynucleotide probes onto a substrate (*e.g.*, glass, nitrocelllose, *etc.*) in a two-dimensional matrix or array having bound probes. The probes can be bound to the substrate by either covalent bonds or by non-specific interactions, such as hydrophobic interactions. Samples of polynucleotides can be detectably labeled (*e.g.*, using radioactive or fluorescent labels) and then hybridized to the probes. Double stranded polynucleotides, comprising the labeled sample polynucleotides bound to probe polynucleotides, can be detected once the unbound portion of the sample is washed away. Techniques for constructing arrays and methods of using these arrays are described in EP No. 0 799 897; PCT No. WO 97/29212; PCT No. WO 97/27317; EP No. 0 785 280; PCT No. WO 97/02357; U.S. Pat. No. 5,593,839; U.S. Pat. No. 5,578,832; EP No. 0 728 520; U.S. Pat. No. 5,599,695; EP No. 0 721 016; U.S. Pat. No. 5,556,752; PCT No. WO 95/22058; and U.S. Pat. No. 5,631,734.

As discussed in some detail above, arrays can be used to examine differential expression of genes and can be used to determine gene function. For example, arrays of the instant polynucleotide sequences can be used to determine if any of the provided polynucleotides are differentially expressed between a test cell and control cell (*e.g.*, cancer cells and normal cells). For example, high expression of a particular message in a cancer cell, which is not observed in a corresponding normal cell, can indicate a cancer specific protein. Exemplary uses of arrays are further described in, for example, Pappalarado *et al.*, *Sem. Radiation Oncol.* (1998) 8:217; and Ramsay *Nature Biotechnol.* (1998) 16:40.

D. <u>Differential Expression</u>

The polynucleotides of the invention can also be used to detect differences in expression levels between two cells, *e.g.*, as a method to identify abnormal or diseased tissue in a human. For polynucleotides corresponding to profiles of protein families as described

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above, the choice of tissue can be selected according to the putative biological function. In general, the expression of a gene corresponding to a specific polynucleotide is compared between a first tissue that is suspected of being diseased and a second, normal tissue of the human. The tissue suspected of being abnormal or diseased can be derived from a different tissue type of the human, but preferably it is derived from the same tissue type; for example an intestinal polyp or other abnormal growth should be compared with normal intestinal tissue. The normal tissue can be the same tissue as that of the test sample, or any normal tissue of the patient, especially those that express the polynucleotide-related gene of interest (e.g., brain, thymus, testis, heart, prostate, placenta, spleen, small intestine, skeletal muscle, pancreas, and the mucosal lining of the colon). A difference between the polynucleotide-related gene, mRNA, or protein in the two tissues which are compared, for example in molecular weight, amino acid or nucleotide sequence, or relative abundance, indicates a change in the gene, or a gene which regulates it, in the tissue of the human that was suspected of being diseased. Examples of detection of differential expression and its use in diagnosis of cancer are described in U.S. Patent Nos. 5,688,641 and 5,677,125.

The polynucleotide-related genes in the two tissues are compared by any means known in the art. For example, the two genes can be sequenced, and the sequence of the gene in the tissue suspected of being diseased compared with the gene sequence in the normal tissue. The genes corresponding to a provided polynucleotide, or portions thereof, in the two tissues are amplified, for example using nucleotide primers based on the nucleotide sequence shown in the Sequence Listing, using the polymerase chain reaction. The amplified genes or portions of genes are hybridized to detectably labeled nucleotide probes selected from a nucleotide sequence shown in the Sequence Listing. A difference in the nucleotide sequence of the isolated gene in the tissue suspected of being diseased compared with the normal nucleotide sequence suggests a role of the gene product encoded by the subject polynucleotide in the disease, and provides guidance for preparing a therapeutic agent.

Alternatively, mRNA corresponding to a provided polynucleotide in the two tissues is compared. PolyA⁺RNA is isolated from the two tissues as is known in the art. For example, one of skill in the art can readily determine differences in the size or amount of mRNA transcripts between the two tissues using Northern blots and detectably labeled

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nucleotide probes selected from the nucleotide sequence shown in the Sequence Listing. Increased or decreased expression of a given mRNA in a tissue sample suspected of being diseased, compared with the expression of the same mRNA in a normal tissue, suggests that the expressed protein has a role in the disease, and also provides a lead for preparing a therapeutic agent.

The comparison can also be accomplished by analyzing polypeptides between the matched samples. The sizes of the proteins in the two tissues are compared, for example, using antibodies of the present invention to detect polypeptides in Western blots of protein extracts from the two tissues. Other changes, such as expression levels and subcellular localization, can also be detected immunologically, using antibodies to the corresponding protein. A higher or lower level of expression of a given polypeptide in a tissue suspected of being diseased, compared with the same protein expression level in a normal tissue, is indicative that the expressed protein has a role in the disease, and provides guidance for preparing a therapeutic agent.

Similarly, comparison of polynucleotide sequences or of gene expression products, *e.g.*, mRNA and protein, between a human tissue that is suspected of being diseased and a normal tissue of a human, are used to follow disease progression or remission in the human. Such comparisons are made as described above. For example, increased or decreased expression of a gene corresponding to an inventive polynucleotide in the tissue suspected of being neoplastic can indicate the presence of neoplastic cells in the tissue. The degree of increased expression of a given gene in the neoplastic tissue relative to expression of the same gene in normal tissue, or differences in the amount of increased expression of a given gene in the neoplastic tissue over time, is used to assess the progression of the neoplasia in that tissue or to monitor the response of the neoplastic tissue to a therapeutic protocol over time.

The expression pattern of any two cell types can be compared, such as low and high metastatic tumor cell lines, malignant or non-malignant cells, or cells from tissue which have and have not been exposed to a therapeutic agent. A genetic predisposition to disease in a human is detected by comparing expression levels of an mRNA or protein corresponding to a polynucleotide of the invention in a fetal tissue with levels associated in normal fetal tissue. Fetal tissues that are used for this purpose include, but are not limited to, amniotic

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fluid, chorionic villi, blood, and the blastomere of an in vitro-fertilized embryo. The comparable normal polynucleotide-related gene is obtained from any tissue. The mRNA or protein is obtained from a normal tissue of a human in which the polynucleotide-related gene is expressed. Differences such as alterations in the nucleotide sequence or size of the same product of the fetal polynucleotide-related gene or mRNA, or alterations in the molecular weight, amino acid sequence, or relative abundance of fetal protein, can indicate a germline mutation in the polynucleotide-related gene of the fetus, which indicates a genetic predisposition to disease. Particular diagnostic and prognostic uses of the disclosed polynucleotides are described in more detail below.

E. <u>Diagnostic</u>, Prognostic, and Other Uses Based On Differential Expression

In general, diagnostic methods of the invention for involve detection of a level or amount of a gene product, particularly a differentially expressed gene product, in a test sample obtained from a patient suspected of having or being susceptible to a disease (e.g., breast cancer, lung cancer, colon cancer and/or metastatic forms thereof), and comparing the detected levels to those levels found in normal cells (e.g., cells substantially unaffected by cancer) and/or other control cells (e.g., to differentiate a cancerous cell from a cell affected by dysplasia). Furthermore, the severity of the disease can be assessed by comparing the detected levels of a differentially expressed gene product with those levels detected in samples representing the levels of differentially gene product associated with varying degrees of severity of disease.

The term "differentially expressed gene" is intended to encompass a polynucleotide that can, for example, include an open reading frame encoding a gene product (*e.g.*, a polypeptide), and/or introns of such genes and adjacent 5' and 3' non-coding nucleotide sequences involved in the regulation of expression, up to about 20 kb beyond the coding region, but possibly further in either direction. The gene can be introduced into an appropriate vector for extrachromosomal maintenance or for integration into a host genome. In general, a difference in expression level associated with a decrease in expression level of at least about 25%, usually at least about 50% to 75%, more usually at least about 90% or more is indicative of a differentially expressed gene of interest, *i.e.*, a gene that is underexpressed or down-regulated in the test sample relative to a control sample. Furthermore, a difference in expression level associated with an increase in expression of at

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least about 25%, usually at least about 50% to 75%, more usually at least about 90% and can be at least about 1 ½-fold, usually at least about 2-fold to about 10-fold, and can be about 100-fold to about 1,000-fold increase relative to a control sample is indicative of a differentially expressed gene of interest, *i.e.*, an overexpressed or up-regulated gene.

"Differentially expressed polynucleotide" as used herein means a nucleic acid molecule (RNA or DNA) having a sequence that represents a differentially expressed gene, e.g., the differentially expressed polynucleotide comprises a sequence (e.g., an open reading frame encoding a gene product) that uniquely identifies a differentially expressed gene so that detection of the differentially expressed polynucleotide in a sample is correlated with the presence of a differentially expressed gene in a sample. "Differentially expressed polynucleotides" is also meant to encompass fragments of the disclosed polynucleotides, e.g., fragments retaining biological activity, as well as nucleic acids homologous, substantially similar, or substantially identical (e.g., having about 90% sequence identity) to the disclosed polynucleotides.

Methods of the subject invention useful in diagnosis or prognosis typically involve comparison of the abundance of a selected differentially expressed gene product in a sample of interest with that of a control to determine any relative differences in the expression of the gene product, where the difference can be measured qualitatively and/or quantitatively. Quantitation can be accomplished, for example, by comparing the level of expression product detected in the sample with the amounts of product present in a standard curve. A comparison can be made visually; by using a technique such as densitometry, with or without computerized assistance; by preparing a representative library of cDNA clones of mRNA isolated from a test sample, sequencing the clones in the library to determine that number of cDNA clones corresponding to the same gene product, and analyzing the number of clones corresponding to that same gene product relative to the number of clones of the same gene product in a control sample; or by using an array to detect relative levels of hybridization to a selected sequence or set of sequences, and comparing the hybridization pattern to that of a control. The differences in expression are then correlated with the presence or absence of an abnormal expression pattern. A variety of different methods for determining the nucleic acid abundance in a sample are known to those of skill in the art, where particular methods of interest include those described in: Pietu et al. Genome Res.

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reference.

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(1996) 6:492; Zhao et al., Gene (1995) 156:207; Soares, Curr. Opin. Biotechnol. (1977) 8:
542; Raval, J. Pharmacol Toxicol Methods (1994) 32:125; Chalifour et al., Anal. Biochem
(1994) 216:299; Stolz et al., Mol. Biotechnol. (1996) 6:225; Hong et al., Biosci. Reports

(1982) 2:907; and McGraw, Anal. Biochem. (1984) 143:298. Also of interest are the methods disclosed in WO 97/27317, the disclosure of which is herein incorporated by

In general, diagnostic assays of the invention involve detection of a gene product of a the polynucleotide sequence (*e.g.*, mRNA or polypeptide) that corresponds to a sequence of SEQ ID NOS:1-844. The patient from whom the sample is obtained can be apparently healthy, susceptible to disease (*e.g.*, as determined by family history or exposure to certain environmental factors), or can already be identified as having a condition in which altered expression of a gene product of the invention is implicated.

In the assays of the invention, the diagnosis can be determined based on detected gene product expression levels of a gene product encoded by at least one, preferably at least two or more, at least 3 or more, or at least 4 or more of the polynucleotides having a sequence set forth in SEQ ID NOS:1-844, and can involve detection of expression of genes corresponding to all of SEQ ID NOS:1-844 and/or additional sequences that can serve as additional diagnostic markers and/or reference sequences. Where the diagnostic method is designed to detect the presence or susceptibility of a patient to cancer, the assay preferably involves detection of a gene product encoded by a gene corresponding to a polynucleotide that is differentially expressed in cancer. For example, a higher level of expression of a polynucleotide corresponding to SEQ ID NO:52 relative to a level associated with a normal sample can indicate the presence of cancer in the patient from whom the sample is derived. In another example, detection of a lower level of a polynucleotide corresponding to SEQ ID NO:39 relative to a normal level is indicative of the presence of cancer in the patient. Further examples of such differentially expressed polynucleotides are described in the Examples below. Given the provided polynucleotides and information regarding their relative expression levels provided herein, assays using such polynucleotides and detection of their expression levels in diagnosis and prognosis will be readily apparent to the ordinarily skilled artisan.

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Any of a variety of detectable labels can be used in connection with the various embodiments of the diagnostic methods of the invention. Suitable detectable labels include fluorochromes, (e.g. fluorescein isothiocyanate (FITC), rhodamine, Texas Red, phycoerythrin, allophycocyanin, 6-carboxyfluorescein (6-FAM), 2',7'-dimethoxy-4',5'-dichloro-6-carboxyfluorescein (JOE), 6-carboxy-X-rhodamine (ROX), 6-carboxy-2',4',7',4,7-hexachlorofluorescein (HEX), 5-carboxyfluorescein (5-FAM) or N,N,N',N'-tetramethyl-6-carboxyrhodamine (TAMRA)), radioactive labels, (e.g. ³²P, ³⁵S, ³H, etc.), and the like. The detectable label can involve a two stage systems (e.g., biotin-avidin, hapten-anti-hapten antibody, etc.)

Reagents specific for the polynucleotides and polypeptides of the invention, such as antibodies and nucleotide probes, can be supplied in a kit for detecting the presence of an expression product in a biological sample. The kit can also contain buffers or labeling components, as well as instructions for using the reagents to detect and quantify expression products in the biological sample. Exemplary embodiments of the diagnostic methods of the invention are described below in more detail.

Polypeptide detection in diagnosis. In one embodiment, the test sample is assayed for the level of a differentially expressed polypeptide. Diagnosis can be accomplished using any of a number of methods to determine the absence or presence or altered amounts of the differentially expressed polypeptide in the test sample. For example, detection can utilize staining of cells or histological sections with labeled antibodies, performed in accordance with conventional methods. Cells can be permeabilized to stain cytoplasmic molecules. In general, antibodies that specifically bind a differentially expressed polypeptide of the invention are added to a sample, and incubated for a period of time sufficient to allow binding to the epitope, usually at least about 10 minutes. The antibody can be detectably labeled for direct detection (e.g., using radioisotopes, enzymes, fluorescers, chemiluminescers, and the like), or can be used in conjunction with a second stage antibody or reagent to detect binding (e.g., biotin with horseradish peroxidase-conjugated avidin, a secondary antibody conjugated to a fluorescent compound, e.g. fluorescein, rhodamine, Texas red, etc.). The absence or presence of antibody binding can be determined by various methods, including flow cytometry of dissociated cells, microscopy, radiography. scintillation counting, etc. Any suitable alternative methods can of qualitative or quantitative

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detection of levels or amounts of differentially expressed polypeptide can be used, for example ELISA, western blot, immunoprecipitation, radioimmunoassay, etc.

In general, the detected level of differentially expressed polypeptide in the test sample is compared to a level of the differentially expressed gene product in a reference or control sample, *e.g.*, in a normal cell (negative control) or in a cell having a known disease state (positive control). For example, a higher level of expression of a polypeptide encoded by SEQ ID NO:52 relative to a level associated with a normal sample can indicate the presence of cancer in the patient from whom the sample is derived. In another example, detection of a lower level of the polypeptide encoded by SEQ ID NO:39 relative to a normal level is indicative of the presence of cancer in the patient.

mRNA detection. The diagnostic methods of the invention can also or alternatively involve detection of mRNA encoded by a gene corresponding to a differentially expressed polynucleotides of the invention. Any suitable qualitative or quantitative methods known in the art for detecting specific mRNAs can be used. mRNA can be detected by, for example, in situ hybridization in tissue sections, by reverse transcriptase-PCR, or in Northern blots containing poly A+ mRNA. One of skill in the art can readily use these methods to determine differences in the size or amount of mRNA transcripts between two samples. For example, the level of mRNA of the invention in a tissue sample suspected of being cancerous or dysplastic is compared with the expression of the mRNA in a reference sample, e.g., a positive or negative control sample (e.g., normal tissue, cancerous tissue, etc.). In a specific non-limiting example, a higher level of mRNA corresponding to SEQ ID NO:52 relative to a level associated with a normal sample can indicate the presence of cancer in the patient from whom the sample is derived. In another example, detection of a lower level of mRNA corresponding to SEQ ID NO:39 relative to a normal level is indicative of the presence of cancer in the patient.

Any suitable method for detecting and comparing mRNA expression levels in a sample can be used in connection with the diagnostic methods of the invention (see, *e.g.*, U.S. 5,804,382). For example, mRNA expression levels in a sample can be determined by generation of a library of expressed sequence tags (ESTs) from the sample, where the EST library is representative of sequences present in the sample (Adams, et al., (1991) *Science* 252:1651). Enumeration of the relative representation of ESTs within the library can be used

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to approximate the relative representation of the gene transcript within the starting sample. The results of EST analysis of a test sample can then be compared to EST analysis of a reference sample to determine the relative expression levels of a selected polynucleotide, particularly a polynucleotide corresponding to one or more of the differentially expressed genes described herein.

Alternatively, gene expression in a test sample can be performed using serial analysis of gene expression (SAGE) methodology (Velculescu et al., *Science* (1995) *270*:484). In short, SAGE involves the isolation of short unique sequence tags from a specific location within each transcript (*e.g.*, a sequence of any one of SEQ ID NOS:1-6). The sequence tags are concatenated, cloned, and sequenced. The frequency of particular transcripts within the starting sample is reflected by the number of times the associated sequence tag is encountered with the sequence population.

Gene expression in a test sample can also be analyzed using differential display (DD) methodology. In DD, fragments defined by specific sequence delimiters (*e.g.*, restriction enzyme sites) are used as unique identifiers of genes, coupled with information about fragment length or fragment location within the expressed gene. The relative representation of an expressed gene with a sample can then be estimated based on the relative representation of the fragment associated with that gene within the pool of all possible fragments. Methods and compositions for carrying out DD are well known in the art, see, *e.g.*, U.S. 5,776,683; and U.S. 5,807,680.

Alternatively, gene expression in a sample using hybridization analysis, which is based on the specificity of nucleotide interactions. Oligonucleotides or cDNA can be used to selectively identify or capture DNA or RNA of specific sequence composition, and the amount of RNA or cDNA hybridized to a known capture sequence determined qualitatively or quantitatively, to provide information about the relative representation of a particular message within the pool of cellular messages in a sample. Hybridization analysis can be designed to allow for concurrent screening of the relative expression of hundreds to thousands of genes by using, for example, array-based technologies having high density formats, including filters, microscope slides, or microchips, or solution-based technologies that use spectroscopic analysis (e.g., mass spectrometry). One exemplary use of arrays in the diagnostic methods of the invention is described below in more detail.

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Use of a single gene in diagnostic applications. The diagnostic methods of the invention can focus on the expression of a single differentially expressed gene. For example, the diagnostic method can involve detecting a differentially expressed gene, or a polymorphism of such a gene (e.g., a polymorphism in an coding region or control region), that is associated with disease. Disease-associated polymorphisms can include deletion or truncation of the gene, mutations that alter expression level and/or affect activity of the encoded protein, etc.

Changes in the promoter or enhancer sequence that affect expression levels of an differentially gene can be compared to expression levels of the normal allele by various methods known in the art. Methods for determining promoter or enhancer strength include quantitation of the expressed natural protein; insertion of the variant control element into a vector with a reporter gene such as β -galactosidase, luciferase, chloramphenicol acetyltransferase, *etc.* that provides for convenient quantitation; and the like.

A number of methods are available for analyzing nucleic acids for the presence of a specific sequence, e.g. a disease associated polymorphism. Where large amounts of DNA are available, genomic DNA is used directly. Alternatively, the region of interest is cloned into a suitable vector and grown in sufficient quantity for analysis. Cells that express a differentially expressed gene can be used as a source of mRNA, which can be assayed directly or reverse transcribed into cDNA for analysis. The nucleic acid can be amplified by conventional techniques, such as the polymerase chain reaction (PCR), to provide sufficient amounts for analysis, and a detectable label can be included in the amplification reaction (e.g., using a detectably labeled primer or detectably labeled oligonucleotides) to facilitate detection. The use of the polymerase chain reaction is described in Saiki, et al., Science (1985) 239:487, and a review of techniques can be found in Sambrook, et al., Molecular Cloning: A Laboratory Manual, (1989) pp. 14.2. Alternatively, various methods are known in the art that utilize oligonucleotide ligation as a means of detecting polymorphisms, for examples see Riley et al., Nucl. Acids Res. (1990) 18:2887; and Delahunty et al., Am. J. Hum. Genet. (1996) 58:1239.

The sample nucleic acid, *e.g.* amplified or cloned fragment, is analyzed by one of a number of methods known in the art. The nucleic acid can be sequenced by dideoxy or other methods, and the sequence of bases compared to a selected sequence, *e.g.*, to a wild-type

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sequence. Hybridization with the polymorphic or variant sequence can also be used to determine its presence in a sample (e.g., by Southern blot, dot blot, etc.). The hybridization pattern of a polymorphic or variant sequence and a control sequence to an array of oligonucleotide probes immobilized on a solid support, as described in US 5,445,934, or in WO 95/35505, can also be used as a means of identifying polymorphic or variant sequences associated with disease. Single strand conformational polymorphism (SSCP) analysis, denaturing gradient gel electrophoresis (DGGE), and heteroduplex analysis in gel matrices are used to detect conformational changes created by DNA sequence variation as alterations in electrophoretic mobility. Alternatively, where a polymorphism creates or destroys a recognition site for a restriction endonuclease, the sample is digested with that endonuclease, and the products size fractionated to determine whether the fragment was digested. Fractionation is performed by gel or capillary electrophoresis, particularly acrylamide or agarose gels.

Screening for mutations in an differentially expressed gene can be based on the functional or antigenic characteristics of the protein. Protein truncation assays are useful in detecting deletions that can affect the biological activity of the protein. Various immunoassays designed to detect polymorphisms in proteins can be used in screening. Where many diverse genetic mutations lead to a particular disease phenotype, functional protein assays have proven to be effective screening tools. The activity of the encoded protein can be determined by comparison with the wild-type protein.

Pattern matching in diagnosis using arrays. In another embodiment, the diagnostic and/or prognostic methods of the invention involve detection of expression of a selected set of genes in a test sample to produce a test expression pattern (TEP). The TEP is compared to a reference expression pattern (REP), which is generated by detection of expression of the selected set of genes in a reference sample (*e.g.*, a positive or negative control sample). The selected set of genes includes at least one of the genes of the invention, which genes correspond to the polynucleotide sequences of SEQ ID NOS:1-844. Of particular interest is a selected set of genes that includes gene differentially expressed in the disease for which the test sample is to be screened.

"Reference sequences" or "reference polynucleotides" as used herein in the context of differential gene expression analysis and diagnosis/prognosis refers to a selected set of

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polynucleotides, which selected set includes at least one or more of the differentially expressed polynucleotides described herein. A plurality of reference sequences, preferably comprising positive and negative control sequences, can be included as reference sequences. Additional suitable reference sequences are found in Genbank, Unigene, and other nucleotide sequence databases (including, *e.g.*, expressed sequence tag (EST), partial, and full-length sequences).

"Reference array" means an array having reference sequences for use in hybridization with a sample, where the reference sequences include all, at least one of, or any subset of the differentially expressed polynucleotides described herein. Usually such an array will include at least 3 different reference sequences, and can include any one or all of the provided differentially expressed sequences. Arrays of interest can further comprise sequences, including polymorphisms, of other genetic sequences, particularly other sequences of interest for screening for a disease or disorder (e.g., cancer, dysplasia, or other related or unrelated diseases, disorders, or conditions). The oligonucleotide sequence on the array will usually be at least about 12 nt in length, and can be of about the length of the provided sequences, or can extend into the flanking regions to generate fragments of 100 nt to 200 nt in length or more.

A "reference expression pattern" or "REP" as used herein refers to the relative levels of expression of a selected set of genes, particularly of differentially expressed genes, that is associated with a selected cell type, *e.g.*, a normal cell, a cancerous cell, a cell exposed to an environmental stimulus, and the like. A "test expression pattern" or "TEP" refers to relative levels of expression of a selected set of genes, particularly of differentially expressed genes, in a test sample (*e.g.*, a cell of unknown or suspected disease state, from which mRNA is isolated).

"Diagnosis" as used herein generally includes determination of a subject's susceptibility to a disease or disorder, determination as to whether a subject is presently affected by a disease or disorder, as well as to the prognosis of a subject affected by a disease or disorder (e.g., identification of pre-metastatic or metastatic cancerous states, stages of cancer, or responsiveness of cancer to therapy). The present invention particularly encompasses diagnosis of subjects in the context of breast cancer (e.g., carcinoma in situ (e.g., ductal carcinoma in situ), estrogen receptor (ER)-positive breast cancer, ER-negative

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breast cancer, or other forms and/or stages of breast cancer), lung cancer (*e.g.*, small cell carcinoma, non-small cell carcinoma, mesothelioma, and other forms and/or stages of lung cancer), and colon cancer (*e.g.*, adenomatous polyp, colorectal carcinoma, and other forms and/or stages of colon cancer).

"Sample" or "biological sample" as used throughout here are generally meant to refer to samples of biological fluids or tissues, particularly samples obtained from tissues, especially from cells of the type associated with the disease for which the diagnostic application is designed (e.g., ductal adenocarcinoma), and the like. "Samples" is also meant to encompass derivatives and fractions of such samples (e.g., cell lysates). Where the sample is solid tissue, the cells of the tissue can be dissociated or tissue sections can be analyzed.

REPs can be generated in a variety of ways according to methods well known in the art. For example, REPs can be generated by hybridizing a control sample to an array having a selected set of polynucleotides (particularly a selected set of differentially expressed polynucleotides), acquiring the hybridization data from the array, and storing the data in a format that allows for ready comparison of the REP with a TEP. Alternatively, all expressed sequences in a control sample can be isolated and sequenced, *e.g.*, by isolating mRNA from a control sample, converting the mRNA into cDNA, and sequencing the cDNA. The resulting sequence information roughly or precisely reflects the identity and relative number of expressed sequences in the sample. The sequence information can then be stored in a format (*e.g.*, a computer-readable format) that allows for ready comparison of the REP with a TEP. The REP can be normalized prior to or after data storage, and/or can be processed to selectively remove sequences of expressed genes that are of less interest or that might complicate analysis (*e.g.*, some or all of the sequences associated with housekeeping genes can be eliminated from REP data).

TEPs can be generated in a manner similar to REPs, *e.g.*, by hybridizing a test sample to an array having a selected set of polynucleotides, particularly a selected set of differentially expressed polynucleotides, acquiring the hybridization data from the array, and storing the data in a format that allows for ready comparison of the TEP with a REP. The REP and TEP to be used in a comparison can be generated simultaneously, or the TEP can be compared to previously generated and stored REPs.

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In one embodiment of the invention, comparison of a TEP with a REP involves hybridizing a test sample with a reference array, where the reference array has one or more reference sequences for use in hybridization with a sample. The reference sequences include all, at least one of, or any subset of the differentially expressed polynucleotides described herein. Hybridization data for the test sample is acquired, the data normalized, and the produced TEP compared with a REP generated using an array having the same or similar selected set of differentially expressed polynucleotides. Probes that correspond to sequences differentially expressed between the two samples will show decreased or increased hybridization efficiency for one of the samples relative to the other.

Reference arrays can be produced according to any suitable methods known in the art. For example, methods of producing large arrays of oligonucleotides are described in U.S. 5,134,854, and U.S. 5,445,934 using light-directed synthesis techniques. Using a computer controlled system, a heterogeneous array of monomers is converted, through simultaneous coupling at a number of reaction sites, into a heterogeneous array of polymers. Alternatively, microarrays are generated by deposition of pre-synthesized oligonucleotides onto a solid substrate, for example as described in PCT published application no. WO 95/35505.

Methods for collection of data from hybridization of samples with a reference arrays are also well known in the art. For example, the polynucleotides of the reference and test samples can be generated using a detectable fluorescent label, and hybridization of the polynucleotides in the samples detected by scanning the microarrays for the presence of the detectable label. Methods and devices for detecting fluorescently marked targets on devices are known in the art. Generally, such detection devices include a microscope and light source for directing light at a substrate. A photon counter detects fluorescence from the substrate, while an x-y translation stage varies the location of the substrate. A confocal detection device that can be used in the subject methods is described in U.S. Patent no. 5,631,734. A scanning laser microscope is described in Shalon et al., *Genome Res.* (1996) 6:639. A scan, using the appropriate excitation line, is performed for each fluorophore used. The digital images generated from the scan are then combined for subsequent analysis. For any particular array element, the ratio of the fluorescent signal from one sample (e.g., a test

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sample) is compared to the fluorescent signal from another sample (e.g., a reference sample), and the relative signal intensity determined.

Methods for analyzing the data collected from hybridization to arrays are well known in the art. For example, where detection of hybridization involves a fluorescent label, data analysis can include the steps of determining fluorescent intensity as a function of substrate position from the data collected, removing outliers, *i.e.* data deviating from a predetermined statistical distribution, and calculating the relative binding affinity of the targets from the remaining data. The resulting data can be displayed as an image with the intensity in each region varying according to the binding affinity between targets and probes.

In general, the test sample is classified as having a gene expression profile corresponding to that associated with a disease or non-disease state by comparing the TEP generated from the test sample to one or more REPs generated from reference samples (*e.g.*, from samples associated with cancer or specific stages of cancer, dysplasia, samples affected by a disease other than cancer, normal samples, *etc.*). The criteria for a match or a substantial match between a TEP and a REP include expression of the same or substantially the same set of reference genes, as well as expression of these reference genes at substantially the same levels (*e.g.*, no significant difference between the samples for a signal associated with a selected reference sequence after normalization of the samples, or at least no greater than about 25% to about 40% difference in signal strength for a given reference sequence. In general, a pattern match between a TEP and a REP includes a match in expression, preferably a match in qualitative or quantitative expression level, of at least one of, all or any subset of the differentially expressed genes of the invention.

Pattern matching can be performed manually, or can be performed using a computer program. Methods for preparation of substrate matrices (*e.g.*, arrays), design of oligonucleotides for use with such matrices, labeling of probes, hybridization conditions, scanning of hybridized matrices, and analysis of patterns generated, including comparison analysis, are described in, for example, U.S. 5,800,992.

F. <u>Use of the Polynucleotides of the Invention in Cancer</u>

Oncogenesis involves the unbridled growth, dedifferentiation and abnormal migration of cells. Cancerous cells can have the ability to compress, invade, and destroy normal tissue. Cancerous cells may also metastasize to other parts of the body via the

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bloodstream or the lymph system and colonize in these other areas. Different cancers are classified by the cell from which the cancerous cell is derived and from its cellular morphology and/or state of differentiation.

Somatic genetic abnormalities cause cancer initiation and progression. Cancer generally is clonally formed, *i.e.* gain of function of oncogenes and loss of function of tumor suppressor genes within a single cell transform the cell to be cancerous, and that single cell grows and divides to form a cancerous lesion. The genes known to be involved in cancer initiation and progression are involved in numerous cellular functions, including developmental differentiation, cell cycle regulation, cell signaling, immunological response, DNA replication, and DNA repair.

The identification and characterization of genetic or biochemical markers in blood or tissues that will detect the earliest changes along the carcinogenesis pathway and monitor the efficacy of various therapies and preventive interventions is a major goal of cancer research. Scientists have identified genetic changes in stool specimens that indicate the stages of colon cancer, and other biomarkers such as gene mutations, hormone receptors, proteins that inhibit metastasis, and enzymes that metabolize drugs are all being used to determine the severity and predict the course of breast, prostate, lung, and other cancers.

Recent advances in the pathogenesis of certain cancers has been helpful in determining patient treatment. The level of expression of certain polynucleotides can be indicative of a poorer prognosis, and therefore warrant more aggressive chemo- or radiotherapy for a patient. The correlation of novel surrogate tumor specific features with response to treatment and outcome in patients has defined certain prognostic indicators that allow the design of tailored therapy based on the molecular profile of the tumor. These therapies include antibody targeting and gene therapy. Moreover, a promising level of one or more marker polynucleotides can provide impetus for not aggressively treating a particular patient, thus sparing the patient the deleterious side effects of aggressive therapy. Determining expression of certain polynucleotides and comparison of a patients profile with known expression in normal tissue and variants of the disease allows a determination of the best possible treatment for a patient, both in terms of specificity of treatment and in terms of comfort level of the patient.

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Surrogate tumor markers, such as polynucleotide expression, can also be used to better classify, and thus diagnose and treat, different forms and disease states of cancer. Two classifications widely used in oncology that can benefit from identification of the expression levels of the polynucleotides of the invention are staging of the cancerous disorder, and grading the nature of the cancerous tissue.

Staging. Staging is a process used by physicians to describe how advanced the cancerous state is in a patient. Staging assists the physician in determining a prognosis, planning treatment and evaluating the results of such treatment. Different staging systems are used for different types of cancer, but each generally involves the following determinations: the type of tumor, indicated by T; whether the cancer has metastasized to nearby lymph nodes, indicated by N; and whether the cancer has metastasized to more distant parts of the body, indicated by M. This system of staging is called the TNM system. Generally, if a cancer is only detectable in the area of the primary lesion without having spread to any lymph nodes it is called Stage I. If it has spread only to the closest lymph nodes, it is called Stage II. In Stage III, the cancer has generally spread to the lymph nodes in near proximity to the site of the primary lesion. Cancers that have spread to a distant part of the body, such as the liver, bone, brain or another site, are called Stage IV, the most advanced stage.

Currently, the determination of staging is done using pathological techniques and is based more on the presence or absence of malignant tissue rather than the characteristics of the tumor type. Presence or absence of malignant tissue is based primarily on the gross morphology of the cells in the areas biopsied. The polynucleotides of the invention can facilitate fine-tuning of the staging process by identifying markers for the aggresivity of a cancer, *e.g.* the metastatic potential, as well as the presence in different areas of the body. Thus, a Stage II cancer with a polynucleotide signifying a high metastatic potential cancer can be used to change a borderline Stage II tumor to a Stage III tumor, justifying more aggressive therapy. Conversely, the presence of a polynucleotide signifying a lower metastatic potential allows more conservative staging of a tumor.

<u>Grading of cancers.</u> Grade is a term used to describe how closely a tumor resembles normal tissue of its same type. Based on the microscopic appearance of a tumor, pathologists will identify the grade of a tumor based on parameters such as cell morphology,

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cellular organization, and other markers of differentiation. As a general rule, the grade of a tumor corresponds to its rate of growth or aggressiveness. That is, undifferentiated or high-grade tumors grow more quickly than well differentiated or low-grade tumors. Information about tumor grade is useful in planning treatment and predicting prognosis.

The American Joint Commission on Cancer has recommended the following guidelines for grading tumors: 1) GX Grade cannot be assessed; 2) G1 Well differentiated; G2 Moderately well differentiated; 3) G3 Poorly differentiated; 4) G4 Undifferentiated. Although grading is used by pathologists to describe most cancers, it plays a more important role in treatment planning for certain types than for others. An example is the Gleason system that is specific for prostate cancer, which uses grade numbers to describe the degree of differentiation. Lower Gleason scores indicate well-differentiated cells. Intermediate scores denote tumors with moderately differentiated cells. Higher scores describe poorly differentiated cells. Grade is also important in some types of brain tumors and soft tissue sarcomas.

The polynucleotides of the invention can be especially valuable in determining the grade of the tumor, as they not only can aid in determining the differentiation status of the cells of a tumor, they can also identify factors other than differentiation that are valuable in determining the aggressivity of a tumor, such as metastatic potential.

<u>Familial Cancer Genes.</u> A number of cancer syndromes are linked to Mendelian inheritance of a predisposition to develop particular cancers. The following table contains a list of cancer types that can be inherited, and for which the gene or genes responsible have been identified. Most of the cancer types listed can occur as part of several different genetic conditions, each caused by alterations in a different gene.

Cancer Type	Genetic Condition	Gene
Brain	Li-Fraumeni syndrome	TP53
	Neurofibromatosis 1	NF1
	Neurofibromatosis 2	NF2
	von Hippel-Lindau syndrome	VHL
	Tuberous sclerosis 2	TSC2
Breast	Hereditary breast/ovarian cancer 1	BRCA1
	Hereditary breast/ovarian cancer 2	BRCA2
	Li-Fraumeni syndrome	TP53
	Ataxia telangiectasia	ATM
Colon	Familial adenomatous polyposis (FAP)	APC
	Hereditary non-polyposis colon cancer (HNPCC) 1	HMSH2
	Hereditary non-polyposis colon cancer (HNPCC) 2	hMLH1

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Cancer Type	Genetic Condition	Gene
• •	Hereditary non-polyposis colon cancer (HNPCC) 3	hPMS1
	Hereditary non-polyposis colon cancer (HNPCC) 4	hPMS2
Endocrine	Multiple endocrine neoplasia 1 (MEN1)	MEN1
(parathyroid, pituitary, GI endocrine)		
Endocrine	Multiple endocrine neoplasia 2 (MEN2)	RET
(pheochromacytoma, medullary thyroid)		
Endometrial	Hereditary non-polyposis colon cancer (HNPCC) 1	hMSH2
	Hereditary non-polyposis colon cancer (HNPCC) 2	hMLH1
	Hereditary non-polyposis colon cancer (HNPCC) 3	hPMS1
	Hereditary non-polyposis colon cancer (HNPCC) 4	hPMS2
Eye	Hereditary retinoblastoma	RB1
Hematologic	Li-Fraumeni syndrome	TP53
(lymphomas and leukemia)		
	Ataxia telangiectasia	ATM
Kidney	Hereditary Wilms' tumor	WT1
	von Hippel-Lindau syndrome	VHL
·	Tuberous sclerosis 2	TSC2
Ovary	Hereditary breast/ovarian cancer 1	BRCA1
•	Hereditary breast/ovarian cancer 2	BRCA2
Sarcoma	Hereditary retinoblastoma	RB1
	Li-Fraumeni syndrome	TP53
	Neurofibromatosis 1	NF1
Skin	Hereditary melanoma 1	CDKN2
	Hereditary melanoma 2	CDK4
	Basal cell naevus (Gorlin) syndrome	PTCH
Stòmach	Hereditary non-polyposis colon cancer (HNPCC) 1	hMSH2
	Hereditary non-polyposis colon cancer (HNPCC) 2	hMLH1
	Hereditary non-polyposis colon cancer (HNPCC) 3	hPMS1
	Hereditary non-polyposis colon cancer (HNPCC) 4	hPMS2

The polynucleotides of the invention can be especially useful to monitor patients having any of the above syndromes to detect potentially malignant events at a molecular level before they are detectable at a gross morphological level. As can be seen from the table, a number of genes are involved in multiple forms of cancer. Thus, a polynucleotide of the invention identified as important for metastatic colon cancer can also have clinical implications for a patient diagnosed with stomach cancer or endometrial cancer.

Lung Cancer. Lung cancer is one of the most common cancers in the United States, accounting for about 15 percent of all cancer cases, or 170,000 new cases each year. At this time, over half of the lung cancer cases in the United States are in men, but the number found in women is increasing and will soon equal that in men. Today more women die of lung cancer than of breast cancer. Lung cancer is especially difficult to diagnose and treat because of the large size of the lungs, which allows cancer to develop for years undetected.

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In fact, lung cancer can spread outside the lungs without causing any symptoms. Adding to the confusion, the most common symptom of lung cancer, a persistent cough, can often be mistaken for a cold or bronchitis.

Although there are more than a dozen different kinds of lung cancer, the two main types of lung cancer are small cell and nonsmall cell, which encompass about 90% of all lung cancer cases. Small cell carcinoma (also called oat cell carcinoma), which usually starts in one of the larger bronchial tubes, grows fairly rapidly, and is likely to be large by the time of diagnosis. Nonsmall cell lung cancer (NSCLC) is made up of three general subtypes of lung cancer. Epidermoid carcinoma (also called squamous cell carcinoma) usually starts in one of the larger bronchial tubes and grows relatively slowly. The size of these tumors can range from very small to quite large. Adenocarcinoma starts growing near the outside surface of the lung and can vary in both size and growth rate. Some slowly growing adenocarcinomas are described as alveolar cell cancer. Large cell carcinoma starts near the surface of the lung, grows rapidly, and the growth is usually fairly large when diagnosed. Other less common forms of lung cancer are carcinoid, cylindroma, mucoepidermoid, and malignant mesothelioma.

Currently, CT scans, MRIs, X-rays, sputum cytology, and biopsies are used to diagnose nonsmall cell lung cancer. The form and cellular origin of the lung cancer is diagnosed primarily through biopsy from either a surgical biopsy or a needle aspiration of lung tissue, and usually the biopsy is prompted from an abnormality identified on an X-ray. In some cases, sputum cytology can reveal lung cancers in patients with normal X-rays or can determine the type of lung cancer, but because it cannot pinpoint the tumor's location, a positive sputum cytology test is usually followed by further tests. Since these tests are based in large part on gross morphology of the tissue, the diagnosis of a particular kind of tumor is largely subjective, and the diagnosis can vary significantly between clinicians.

The polynucleotides of the invention can be used to distinguish types of lung cancer as well as identifying traits specific to a certain patient's cancer. For example, if the patient's biopsy expresses a polynucleotide that is associated with a low metastatic potential, it may justify leaving a larger portion of the patient's lung in surgery to remove the lesion.

Alternatively, a smaller lesion with expression of a polynucleotide that is associated with high metastatic potential may justify a more radical removal of lung tissue and/or the

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Similarly, the expression of polynucleotides of the invention can be used in the diagnosis, prognosis and management of colorectal cancer. The differential expression of a polynucleotide in hyperplasia can be used as a diagnostic marker for metastatic lung cancer. The polynucleotides of the invention that would be especially useful for this purpose are those that exhibit differential expression between high metastatic versus low metastatic lung cancer , *i.e.* SEQ ID NOS: 9, 34, 42, 62, 74, 106, 119, 135, 154, 160, 260, 308, 323, 349, 361, 369, 371, 381, 395, and 400. Detection of malignant lung cancer with a higher metastatic potential can be determined using expression levels of any of these sequences alone or in combination with the levels of expression of other known genes.

Breast Cancer. The National Cancer Institute (NCI) estimates that about 1 in 8 women in the United States will develop breast cancer during her lifetime. Clinical breast examination and mammography are recommended as combined modalities for breast cancer screening, and the nature of the cancer will often depend upon the location of the tumor and the cell type from which the tumor is derived. The majority of breast cancers are adenocarcinomas subtypes, which can be summarized as follows:

Ductal carcinoma in situ (DCIS): Ductal carcinoma in situ is the most common type of noninvasive breast cancer. In DCIS, the malignant cells have not metastasized through the walls of the ducts into the fatty tissue of the breast. Comedocarcinoma is a type of DCIS that is more likely than other types of DCIS to come back in the same area after lumpectomy. It is more closely linked to eventual development of invasive ductal carcinoma than other forms of DCIS.

Infiltrating (or invasive) ductal carcinoma (IDC): this type of cancer has metastasized through the wall of the duct and invaded the fatty tissue of the breast. At this point, it has the potential to use the lymphatic system and bloodstream for metastasis to more distant parts of the body. Infiltrating ductal carcinoma accounts for about 80% of breast cancers.

Lobular carcinoma in situ (LCIS): While not a true cancer, LCIS (also called lobular neoplasia) is sometimes classified as a type of noninvasive breast cancer. It does not penetrate through the wall of the lobules. Although it does not itself usually become an

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invasive cancer, women with this condition have a higher risk of developing an invasive breast cancer in the same breast, or in the opposite breast.

Infiltrating (or invasive) lobular carcinoma (ILC): ILC is similar to IDC, in that it has the potential metastasize elsewhere in the body. About 10% to 15% of invasive breast cancers are invasive lobular carcinomas. ILC can be more difficult to detect by mammogram than IDC.

Inflammatory breast cancer: This rare type of invasive breast cancer accounts for about 1% of all breast cancers and is extremely aggressive. Multiple skin symptoms associated with this cancer are caused by cancer cells blocking lymph vessels or channels in the skin over the breast.

Medullary carcinoma: This special type of infiltrating breast cancer has a relatively well defined, distinct boundary between tumor tissue and normal tissue. It accounts for about 5% of breast cancers. The prognosis for this kind of breast cancer is better than for other types of invasive breast cancer.

Mucinous carcinoma: This rare type of invasive breast cancer originates from mucusproducing cells. The prognosis for mucinous carcinoma is better than for the more common types of invasive breast cancer.

Paget's disease of the nipple: This type of breast cancer starts in the ducts and spreads to the skin of the nipple and the areola. It is a rare type of breast cancer, occurring in only 1% of all cases. Paget's disease can be associated with in situ carcinoma, or with infiltrating breast carcinoma. If no lump can be felt in the breast tissue, and the biopsy shows DCIS but no invasive cancer, the prognosis is excellent.

Phyllodes tumor: This very rare type of breast tumor forms from the stroma of the breast, in contrast to carcinomas which develop in the ducts or lobules. Phyllodes (also spelled phylloides) tumors are usually benign, but are malignant on rare occasions. Nevertheless, malignant phyllodes tumors are very rare and less than 10 women per year in the US die of this disease. Benign phyllodes tumors are successfully treated by removing the mass and a narrow margin of normal breast tissue.

Tubular carcinoma: Accounting for about 2% of all breast cancers, tubular carcinomas are a special type of infiltrating breast carcinoma. They have a better prognosis than usual infiltrating ductal or lobular carcinomas.

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High-quality mammography combined with clinical breast exam remains the only screening method clearly tied to reduction in breast cancer mortality. Lower dose x-rays, digitized computer rather than film images, and the use of computer programs to assist diagnosis, are almost ready for widespread dissemination. Other technologies also are being developed, including magnetic resonance imaging and ultrasound. In addition, a very low radiation exposure technique, positron emission tomography has the potential for detecting early breast cancer.

It is also possible to differentiate between non-cancerous breast tissue and malignant breast tissue by analyzing differential gene expression between tissues. In addition, there may be several possible alterations that lead to the various possible types of breast cancer. The different types of breast tumors (e.g., invasive vs. non-invasive, ductal vs. axillary lymph node) can be differentiable from one another by the identification of the differences in genes expressed by different types of breast tumor tissues (Porter-Jordan et al., Hematol Oncol Clin North Am (1994) 8:73). Breast cancer can thus be generally diagnosed by detection of expression of a gene or genes associated with breast tumors. Where enough information is available about the differential gene expression between various types of breast tumor tissues, the specific type of breast tumor can also be diagnosed.

For example, increased estrogen receptor (ER) expression in normal breast epithileum, while not itself indicative of malignant tissue, is a known risk marker for development of breast cancer. Khan SA *et al.*, *Cancer Res* (1994) *54*:993. Malignant breast cancer is often divided into two groups, ER-positive and ER-negative, based on the estrogen receptor status of the tissue. The ER status represents different survival length and response to hormone therapy, and is thought to represent either: 1) an indicator of different stages of the disease, or 2) an indicator that allows differentiation between two similar but distinct diseases. K. Zhu *et al.*, *Med. Hypoth.* (1997) *49*:69. A number of other genes are known to vary expression between either different stages of cancer or different types of similar breast cancer.

Similarly, the expression of polynucleotides of the invention can be used in the diagnosis and management of breast cancer. The differential expression of a polynucleotide in human breast tumor tissue can be used as a diagnostic marker for human breast cancer. The polynucleotides of the invention that would be especially useful for this purpose are

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those that exhibit differential expression between breast cancer tissue with a high metastatic potential and a low metastatic potential, *i.e.* SEQ ID NOS: 9, 42, 52, 62, 65, 66, 68, 114, 123, 144, 172, 178, 214, 219, 223, 258, 317, and 379. Detection of breast cancer can be determined using expression levels of any of these sequences alone or in combination.

Determination of the aggressive nature and/or the metastatic potential of a breast cancer can also be determined by comparing levels of one or more polynucleotides of the invention and comparing levels of another sequence known to vary in cancerous tissue, *e.g.* ER expression. In addition, development of breast cancer can be detected by examining the ratio of SEQ ID NO: to the levels of steroid hormones (*e.g.*, testosterone or estrogen) or to other hormones (*e.g.*, growth hormone, insulin). Thus expression of specific marker polynucleotides can be used to discriminate between normal and cancerous breast tissue, to discriminate between breast cancers with different cells of origin, to discriminate between breast cancers with different potential metastatic rates, etc.

Diagnosis of breast cancer can also involve comparing the expression of a polynucleotide of the invention with the expression of other sequences in non-malignant breast tissue samples in comparison to one or more forms of the diseased tissue. A comparison of expression of one or more polynucleotides of the invention between the samples provides information on relative levels of these polynucleotides as well as the ratio of these polynucleotides to the expression of other sequences in the tissue of interest compared to normal.

This risk of breast cancer is elevated significantly by the presence of an inherited risk for breast cancer, such as a mutation in BRCA-1 or BRCA-2. New diagnostic tools are being developed to address the needs of higher risk patients to complement mammography and physical examinations for early detection of breast cancer, particularly among younger women. The presence of antigen or expression markers in nipple aspirate fluid (NAF) samples collected from one or both breasts can be useful for useful for risk assessment or early cancer detection. Breast cytology and biomarkers obtained by random fine needle aspiration have been used to identify hyperplasia with atypia and overexpression of p53 and EGFR. The polynucleotides of the invention can be used in multivariate analysis with expression studies with genes such as p53 and EGFR as risk predictors and as surrogate endpoint biomarkers for breast cancer.

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As well as being used for diagnosis and risk assessment, the expression of certain genes can also correlated to prognosis of a disease state. The expression of particular gene have been used as prognostic indicators for breast cancer including increased expression of c-erbB-2, pS2, ER, progesterone receptor, epidermal growth factor receptor (EGFR), neu, myc, bcl-2, int2, cytosolic tyrosine kinase, cyclin E, prad-1, hst, uPA, PAI-1, PAI-2, cathepsin D, as well as the presence of a number of cancer-specific antigens, e.g. CEA, CA M26, CA M29 and CA 15.3. Davis, Br. J. Biomed Sci. (1996) 53:157. Poor prognosis has also been linked to a decrease in expression of certain genes, such as p53, Rb, nm23. The expression of the polynucleotides of the invention can be of prognostic value for determining the metastatic potential of a malignant breast cancer, as this molecules are differentially expressed between high and low metastatic potential tissues tumors. The levels of these polynucleotides in patients with malignant breast cancer can compared to normal tissue. malignant tissue with a known high potential metastatic level, and malignant tissue with a known lower level of metastatic potential to provide a prognosis for a particular patient. Such a prognosis is predictive of the extent and nature of the cancer. The determined prognosis is useful in determining the prognosis of a patient with breast cancer, both for initial treatment of the disease and for longer-term monitoring of the same patient. If samples are taken from the same individual over a period of time, differences in polynucleotide expression that are specific to that patient can be identified and closely watched.

Colon Cancer. Colorectal cancer is one of the most common neoplasms in humans and perhaps the most frequent form of hereditary neoplasia. Prevention and early detection are key factors in controlling and curing colorectal cancer. Indeed, colorectal cancer is the second most preventable cancer, after lung cancer. Colorectal cancer begins as polyps, which are small, benign growths of cells that form on the inner lining of the colon. Over a period of several years, some of these polyps accumulate additional mutations and become cancerous. About 20 percent of all cases of colon cancer are thought to be related to heredity. Currently, multiple familial colorectal cancer disorders have been identified, which are summarized as follows:

Familial adenomatous polyposis (FAP): This condition results in a person having hundreds or even thousands of polyps in the colon and rectum that usually first appear during

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the teenage years. Cancer nearly always develops in one or more of these polyps between the ages of 30 and 50.

Gardner's syndrome: Like FAP, Gardner's syndrome results in polyps and colorectal cancers that develop at a young age. It can also cause benign tumors of the skin, soft connective tissue and bones.

Hereditary nonpolyposis colon cancer (HNPCC): People with this condition tend to develop colorectal cancer at a young age, without first having many polyps. HNPCC has an autosomal dominant pattern of inheritance with variable but high penetrance estimated to be about 90%. HNPCC underlies 0.5%-10% of all cases of colorectal cancer. An understanding of the mechanisms behind the development of HNPCC is emerging, and genetic presymptomatic testing, now being conducted in research settings, soon will be available on a widespread basis for individuals identified at risk for this disease.

Familial colorectal cancer in Ashkenazi Jews: Recent research has found an inherited tendency to developing colorectal cancer among some Jews of Eastern European descent. Like people with FAP, Gardner's syndrome, and HNPCC, their increased risk is due to an inherited mutation present in about 6% of American Jews.

Several tests are currently used to screen for colorectal cancer, including digital rectal examination, fecal occult blood test, sigmoidoscopy, colonoscopy, virtual colonoscopy and MRI. Each of these tests identifies potential colorectal cancer lesions, or a risk of development of these lesions, at a fairly gross morphological level.

The sequential alteration of a number of genes is associated with malignant adenocarcinoma, including the genes DCC, p53, ras, and FAP. For a review, see *e.g.* Fearon ER, *et al.*, *Cell* (1990) *61(5)*:759; Hamilton SR *et al.*, *Cancer* (1993) 72:957; Bodmer W, *et al.*, *Nat Genet.* (1994) 4(3):217; Fearon ER, *Ann N Y Acad Sci.* (1995) 768:101. Molecular genetic alterations are thus promising as potential diagnostic and prognostic indicators in colorectal carcinoma and molecular genetics of colorectal carcinoma since it is possible to differentiate between different types of colorectal neoplasias using molecular markers. Colorectal cancer can thus be generally diagnosed by detection of expression of a gene or genes associated with colorectal tumors.

Similarly, the expression of polynucleotides of the invention can be used in the diagnosis, prognosis and management of colorectal cancer. The differential expression of a

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polynucleotide in hyperplasia can be used as a diagnostic marker for colon cancer. The polynucleotides of the invention that would be especially useful for this purpose are those that exhibit differential expression between malignant metastatic colon cancer and normal patient tissue, *i.e.* SEQ ID NOS: 52, 119, 172, 288. Detection of malignant colon cancer can be determined using expression levels of any of these sequences alone or in combination with the levels of expression.

Determination of the aggressive nature and/or the metastatic potential of a colon cancer can also be determined by comparing levels of one or more polynucleotides of the invention and comparing total levels of another sequence known to vary in cancerous tissue, e.g. p53 expression. In addition, development of colon cancer can be detected by examining the ratio of any of the polynucleotides of the invention to the levels of oncogenes (e.g. ras) or tumor suppressor genes (e.g. FAP or p53). Thus expression of specific marker polynucleotides can be used to discriminate between normal and cancerous breast tissue, to discriminate between breast cancers with different cells of origin, to discriminate between breast cancers with different rates, etc.

G. <u>Use of Polynucleotides to Screen for Peptide Analogs and Antagonists</u>

Polypeptides encoded by the instant polynucleotides and corresponding full length genes can be used to screen peptide libraries to identify binding partners, such as receptors, from among the encoded polypeptides.

A library of peptides can be synthesized following the methods disclosed in U.S. Pat. No. 5,010,175 ('175), and in WO 91/17823. As described below in brief, one prepares a mixture of peptides, which is then screened to identify the peptides exhibiting the desired signal transduction and receptor binding activity. In the '175 method, a suitable peptide synthesis support (e.g., a resin) is coupled to a mixture of appropriately protected, activated amino acids. The concentration of each amino acid in the reaction mixture is balanced or adjusted in inverse proportion to its coupling reaction rate so that the product is an equimolar mixture of amino acids coupled to the starting resin. The bound amino acids are then deprotected, and reacted with another balanced amino acid mixture to form an equimolar mixture of all possible dipeptides. This process is repeated until a mixture of peptides of the desired length (e.g., hexamers) is formed. Note that one need not include all amino acids in each step: one can include only one or two amino acids in some steps (e.g., where it is

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known that a particular amino acid is essential in a given position), thus reducing the complexity of the mixture. After the synthesis of the peptide library is completed, the mixture of peptides is screened for binding to the selected polypeptide. The peptides are then tested for their ability to inhibit or enhance activity. Peptides exhibiting the desired activity are then isolated and sequenced.

The method described in WO 91/17823 is similar. However, instead of reacting the synthesis resin with a mixture of activated amino acids, the resin is divided into twenty equal portions (or into a number of portions corresponding to the number of different amino acids to be added in that step), and each amino acid is coupled individually to its portion of resin.

The resin portions are then combined, mixed, and again divided into a number of equal portions for reaction with the second amino acid. In this manner, each reaction can be easily driven to completion. Additionally, one can maintain separate "subpools" by treating portions in parallel, rather than combining all resins at each step. This simplifies the process of determining which peptides are responsible for any observed receptor binding or signal transduction activity.

In such cases, the subpools containing, *e.g.*, 1-2,000 candidates each are exposed to one or more polypeptides of the invention. Each subpool that produces a positive result is then resynthesized as a group of smaller subpools (sub-subpools) containing, *e.g.*, 20-100 candidates, and reassayed. Positive sub-subpools can be resynthesized as individual compounds, and assayed finally to determine the peptides that exhibit a high binding constant. These peptides can be tested for their ability to inhibit or enhance the native activity. The methods described in WO 91/7823 and U.S. Patent No. 5,194,392 (herein incorporated by reference) enable the preparation of such pools and subpools by automated techniques in parallel, such that all synthesis and resynthesis can be performed in a matter of days.

Peptide agonists or antagonists are screened using any available method, such as signal transduction, antibody binding, receptor binding, mitogenic assays, chemotaxis assays, etc. The methods described herein are presently preferred. The assay conditions ideally should resemble the conditions under which the native activity is exhibited *in vivo*, that is, under physiologic pH, temperature, and ionic strength. Suitable agonists or antagonists will exhibit strong inhibition or enhancement of the native activity at

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concentrations that do not cause toxic side effects in the subject. Agonists or antagonists that compete for binding to the native polypeptide can require concentrations equal to or greater than the native concentration, while inhibitors capable of binding irreversibly to the polypeptide can be added in concentrations on the order of the native concentration.

The end results of such screening and experimentation will be at least one novel polypeptide binding partner, such as a receptor, encoded by a gene or a cDNA corresponding to a polynucleotide of the invention, and at least one peptide agonist or antagonist of the novel binding partner. Such agonists and antagonists can be used to modulate, enhance, or inhibit receptor function in cells to which the receptor is native, or in cells that possess the receptor as a result of genetic engineering. Further, if the novel receptor shares biologically important characteristics with a known receptor, information about agonist/antagonist binding can facilitate development of improved agonists/antagonists of the known receptor.

H. Pharmaceutical Compositions and Therapeutic Uses

Pharmaceutical compositions can comprise polypeptides, antibodies, or polynucleotides of the claimed invention. The pharmaceutical compositions will comprise a therapeutically effective amount of either polypeptides, antibodies, or polynucleotides of the claimed invention.

The term "therapeutically effective amount" as used herein refers to an amount of a therapeutic agent to treat, ameliorate, or prevent a desired disease or condition, or to exhibit a detectable therapeutic or preventative effect. The effect can be detected by, for example, chemical markers or antigen levels. Therapeutic effects also include reduction in physical symptoms, such as decreased body temperature. The precise effective amount for a subject will depend upon the subject's size and health, the nature and extent of the condition, and the therapeutics or combination of therapeutics selected for administration. Thus, it is not useful to specify an exact effective amount in advance. However, the effective amount for a given situation is determined by routine experimentation and is within the judgment of the clinician. For purposes of the present invention, an effective dose will generally be from about 0.01 mg/kg to 50 mg/kg or 0.05 mg/kg to about 10 mg/kg of the DNA constructs in the individual to which it is administered.

A pharmaceutical composition can also contain a pharmaceutically acceptable carrier. The term "pharmaceutically acceptable carrier" refers to a carrier for administration of a

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therapeutic agent, such as antibodies or a polypeptide, genes, and other therapeutic agents. The term refers to any pharmaceutical carrier that does not itself induce the production of antibodies harmful to the individual receiving the composition, and which can be administered without undue toxicity. Suitable carriers can be large, slowly metabolized macromolecules such as proteins, polysaccharides, polylactic acids, polyglycolic acids, polymeric amino acids, amino acid copolymers, and inactive virus particles. Such carriers are well known to those of ordinary skill in the art.

Pharmaceutically acceptable salts can be used therein, for example, mineral acid salts such as hydrochlorides, hydrobromides, phosphates, sulfates, and the like; and the salts of organic acids such as acetates, propionates, malonates, benzoates, and the like. A thorough discussion of pharmaceutically acceptable excipients is available in *Remington's Pharmaceutical Sciences* (Mack Pub. Co., N.J. 1991).

Pharmaceutically acceptable carriers in therapeutic compositions can include liquids such as water, saline, glycerol and ethanol. Auxiliary substances, such as wetting or emulsifying agents, pH buffering substances, and the like, can also be present in such vehicles. Typically, the therapeutic compositions are prepared as injectables, either as liquid solutions or suspensions; solid forms suitable for solution in, or suspension in, liquid vehicles prior to injection can also be prepared. Liposomes are included within the definition of a pharmaceutically acceptable carrier.

Delivery Methods. Once formulated, the compositions of the invention can be (1) administered directly to the subject (*e.g.*, as polynucleotide or polypeptides); (2) delivered ex vivo, to cells derived from the subject (*e.g.*, as in *ex vivo* gene therapy); or (3) delivered *in vitro* for expression of recombinant proteins (*e.g.*, polynucleotides). Direct delivery of the compositions will generally be accomplished by injection, either subcutaneously, intraperitoneally, intravenously or intramuscularly, or delivered to the interstitial space of a tissue. The compositions can also be administered into a tumor or lesion. Other modes of administration include oral and pulmonary administration, suppositories, and transdermal applications, needles, and gene guns or hyposprays. Dosage treatment can be a single dose schedule or a multiple dose schedule.

Methods for the ex vivo delivery and reimplantation of transformed cells into a subject are known in the art and described in *e.g.*, International Publication No. WO

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93/14778. Examples of cells useful in ex vivo applications include, for example, stem cells, particularly hematopoetic, lymph cells, macrophages, dendritic cells, or tumor cells. Generally, delivery of nucleic acids for both ex vivo and in vitro applications can be accomplished by, for example, dextran-mediated transfection, calcium phosphate precipitation, polybrene mediated transfection, protoplast fusion, electroporation, encapsulation of the polynucleotide(s) in liposomes, and direct microinjection of the DNA into nuclei, all well known in the art.

Once a gene corresponding to a polynucleotide of the invention has been found to correlate with a proliferative disorder, such as neoplasia, dysplasia, and hyperplasia, the disorder can be amenable to treatment by administration of a therapeutic agent based on the provided polynucleotide or corresponding polypeptide.

Preparation of antisense polynucleotides is discussed above. Neoplasias that are treated with the antisense composition include, but are not limited to, cervical cancers, melanomas, colorectal adenocarcinomas, Wilms' tumor, retinoblastoma, sarcomas, myosarcomas, lung carcinomas, leukemias, such as chronic myelogenous leukemia, promyelocytic leukemia, monocytic leukemia, and myeloid leukemia, and lymphomas, such as histiocytic lymphoma. Proliferative disorders that are treated with the therapeutic composition include disorders such as anhydric hereditary ectodermal dysplasia, congenital alveolar dysplasia, epithelial dysplasia of the cervix, fibrous dysplasia of bone, and mammary dysplasia. Hyperplasias, for example, endometrial, adrenal, breast, prostate, or thyroid hyperplasias or pseudoepitheliomatous hyperplasia of the skin, are treated with antisense therapeutic compositions based upon a polynucleotide of the invention. Even in disorders in which mutations in the corresponding gene are not implicated, downregulation or inhibition of expression of a gene corresponding to a polynucleotide of the invention can have therapeutic application. For example, decreasing gene expression can help to suppress tumors in which enhanced expression of the gene is implicated.

Both the dose of the antisense composition and the means of administration are determined based on the specific qualities of the therapeutic composition, the condition, age, and weight of the patient, the progression of the disease, and other relevant factors.

Administration of the therapeutic antisense agents of the invention includes local or systemic administration, including injection, oral administration, particle gun or catheterized

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wo 99/33982 PCT/US98/27610 administration, and topical administration. Preferably, the therapeutic antisense composition contains an expression construct comprising a promoter and a polynucleotide segment of at least 12, 22, 25, 30, or 35 contiguous nucleotides of the antisense strand of a polynucleotide disclosed herein. Within the expression construct, the polynucleotide segment is located downstream from the promoter, and transcription of the polynucleotide segment initiates at the promoter.

Various methods are used to administer the therapeutic composition directly to a specific site in the body. For example, a small metastatic lesion is located and the therapeutic composition injected several times in several different locations within the body of tumor. Alternatively, arteries which serve a tumor are identified, and the therapeutic composition injected into such an artery, in order to deliver the composition directly into the tumor. A tumor that has a necrotic center is aspirated and the composition injected directly into the now empty center of the tumor. The antisense composition is directly administered to the surface of the tumor, for example, by topical application of the composition. X-ray imaging is used to assist in certain of the above delivery methods.

Receptor-mediated targeted delivery of therapeutic compositions containing an antisense polynucleotide, subgenomic polynucleotides, or antibodies to specific tissues is also used. Receptor-mediated DNA delivery techniques are described in, for example, Findeis et al., Trends Biotechnol. (1993) 11:202; Chiou et al., Gene Therapeutics: Methods And Applications Of Direct Gene Transfer (J.A. Wolff, ed.) (1994); Wu et al., J. Biol. Chem. (1988) 263:621; Wu et al., J. Biol. Chem. (1994) 269:542; Zenke et al., Proc. Natl. Acad. Sci. (USA) (1990) 87:3655; Wu et al., J. Biol. Chem. (1991) 266:338. Preferably, receptor-mediated targeted delivery of therapeutic compositions containing antibodies of the invention is used to deliver the antibodies to specific tissue.

Therapeutic compositions containing antisense subgenomic polynucleotides are administered in a range of about 100 ng to about 200 mg of DNA for local administration in a gene therapy protocol. Concentration ranges of about 500 ng to about 50 mg, about 1 μ g to about 2 mg, about 5 μ g to about 500 μ g, and about 20 μ g to about 100 μ g of DNA can also be used during a gene therapy protocol. Factors such as method of action and efficacy of transformation and expression are considerations which will affect the dosage required for ultimate efficacy of the antisense subgenomic polynucleotides. Where greater expression is

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desired over a larger area of tissue, larger amounts of antisense subgenomic polynucleotides or the same amounts readministered in a successive protocol of administrations, or several administrations to different adjacent or close tissue portions of, for example, a tumor site, may be required to effect a positive therapeutic outcome. In all cases, routine experimentation in clinical trials will determine specific ranges for optimal therapeutic effect. A more complete description of gene therapy vectors, especially retroviral vectors, is contained in U.S. Serial No. 08/869,309, which is expressly incorporated herein, and in section G below.

For polynucleotide-related genes encoding polypeptides or proteins with anti-inflammatory activity, suitable use, doses, and administration are described in U.S. Patent No. 5,654,173. Therapeutic agents also include antibodies to proteins and polypeptides encoded by the polynucleotides of the invention and related genes, as described in U.S. Patent No. 5,654,173.

I. Gene Therapy

The therapeutic polynucleotides and polypeptides of the present invention can be utilized in gene delivery vehicles. The gene delivery vehicle can be of viral or non-viral origin (see generally, Jolly, *Cancer Gene Therapy* (1994) 1:51; Kimura, *Human Gene Therapy* (1994) 5:845; Connelly, *Human Gene Therapy* (1995) 1:185; and Kaplitt, *Nature Genetics* (1994) 6:148). Gene therapy vehicles for delivery of constructs including a coding sequence of a therapeutic of the invention can be administered either locally or systemically. These constructs can utilize viral or non-viral vector approaches. Expression of such coding sequences can be induced using endogenous mammalian or heterologous promoters. Expression of the coding sequence can be either constitutive or regulated.

The present invention can employ recombinant retroviruses which are constructed to carry or express a selected nucleic acid molecule of interest. Retrovirus vectors that can be employed include those described in EP 0 415 731; WO 90/07936; WO 94/03622; WO 93/25698; WO 93/25234; U.S. Patent No. 5, 219,740; WO 93/11230; WO 93/10218; Vile and Hart, Cancer Res. (1993) 53:3860; Vile et al., Cancer Res. (1993) 53:962; Ram et al., Cancer Res. (1993) 53:83; Takamiya et al., J. Neurosci. Res. (1992) 33:493; Baba et al., J. Neurosurg. (1993) 79:729; U.S. Patent No. 4,777,127; GB Patent No. 2,200,651; and EP 0 345 242. Preferred recombinant retroviruses include those described in WO 91/02805.

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Packaging cell lines suitable for use with the above-described retroviral vector constructs can be readily prepared (see, *e.g.*, WO 95/30763 and WO 92/05266), and used to create producer cell lines (also termed vector cell lines) for the production of recombinant vector particles. Within particularly preferred embodiments of the invention, packaging cell lines are made from human (such as HT1080 cells) or mink parent cell lines, thereby allowing production of recombinant retroviruses that can survive inactivation in human serum.

The present invention also employs alphavirus-based vectors that can function as gene delivery vehicles. Such vectors can be constructed from a wide variety of alphaviruses, including, for example, Sindbis virus vectors, Semliki forest virus (ATCC VR-67; ATCC VR-1247), Ross River virus (ATCC VR-373; ATCC VR-1246) and Venezuelan equine encephalitis virus (ATCC VR-923; ATCC VR-1250; ATCC VR 1249; ATCC VR-532). Representative examples of such vector systems include those described in U.S. Patent Nos. 5,091,309; 5,217,879; and 5,185,440; WO 92/10578; WO 94/21792; WO 95/27069; WO 95/27044; and WO 95/07994. Gene delivery vehicles of the present invention can also employ parvovirus such as adeno-associated virus (AAV) vectors. Representative examples include the AAV vectors disclosed by Srivastava in WO 93/09239, Samulski et al., *J. Virol.* (1989) 63:3822; Mendelson et al., *Virol.* (1988) 166:154; and Flotte et al., PNAS (1993) 90:10613.

Representative examples of adenoviral vectors include those described by Berkner, Biotechniques (1988) 6:616; Rosenfeld et al., Science (1991) 252:431; WO 93/19191; Kolls et al., PNAS (1994) 91:215; Kass-Eisler et al., PNAS (1993) 90:11498; Guzman et al., Circulation (1993) 88:2838; Guzman et al., Cir. Res. (1993) 73:1202; Zabner et al., Cell (1993) 75:207; Li et al., Hum. Gene Ther. (1993) 4:403; Cailaud et al., Eur. J. Neurosci. (1993) 5:1287; Vincent et al., Nat. Genet. (1993) 5:130; Jaffe et al., Nat. Genet. (1992) 1:372; and Levrero et al., Gene (1991) 101:195. Exemplary adenoviral gene therapy vectors employable in this invention also include those described in WO 94/12649, WO 93/03769; WO 93/19191; WO 94/28938; WO 95/11984 and WO 95/00655. Administration of DNA linked to killed adenovirus as described in Curiel, Hum. Gene Ther. (1992) 3:147 can be employed.

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Other gene delivery vehicles and methods can be employed, including polycationic condensed DNA linked or unlinked to killed adenovirus alone, for example Curiel, *Hum. Gene Ther.* (1992) 3:147; ligand linked DNA, for example see Wu, *J. Biol. Chem.* (1989) 264:16985; eukaryotic cell delivery vehicles cells, for example see U.S. Pat. No. 5,814,482; WO 95/07994; WO 96/17072; WO 95/30763; and WO 97/42338; deposition of photopolymerized hydrogel materials; hand-held gene transfer particle gun, as described in U.S. Patent No. 5,149,655; ionizing radiation as described in U.S. Patent No. 5,206,152 and in WO92/11033; nucleic charge neutralization or fusion with cell membranes. Additional approaches are described in Philip, *Mol. Cell Biol.* (1994) 14:2411, and in Woffendin, *Proc. Natl. Acad. Sci.* (1994) 91:1581.

Naked DNA can also be employed. Exemplary naked DNA introduction methods are described in WO 90/11092 and U.S. Patent No. 5,580,859. Uptake efficiency can be improved using biodegradable latex beads. DNA coated latex beads are efficiently transported into cells after endocytosis initiation by the beads. The method can be improved further by treatment of the beads to increase hydrophobicity and thereby facilitate disruption of the endosome and release of the DNA into the cytoplasm. Liposomes that can act as gene delivery vehicles are described in U.S. Patent No. 5,422,120; WO 95/13796; WO 94/23697; WO 91/14445; and EP 0524968.

Further non-viral delivery suitable for use includes mechanical delivery systems such as the approach described in Woffendin *et al.*, *Proc. Natl. Acad. Sci. USA* (1994) 91(24):11581. Moreover, the coding sequence and the product of expression of such can be delivered through deposition of photopolymerized hydrogel materials. Other conventional methods for gene delivery that can be used for delivery of the coding sequence include, for example, use of hand-held gene transfer particle gun, as described in U.S. Patent No.

5,149,655; use of ionizing radiation for activating transferred gene, as described in U.S. Patent No. 5,206,152 and WO 92/11033.

The present invention will now be illustrated by reference to the following examples which set forth particularly advantageous embodiments. However, it should be noted that these embodiments are illustrative and are not to be construed as restricting the invention in any way.

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EXAMPLES

The present invention is now illustrated by reference to the following examples which set forth particularly advantageous embodiments. However, these embodiments are illustrative and are not meant to be construed as restricting the invention in any way.

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Example 1: Source of Biological Materials and Overview of Novel Polynucleotides Expressed by the Biological Materials

Human colon cancer cell line Km12L4-A (Morika, W. A. K. et al., Cancer Research (1988) 48:6863) was used to construct a cDNA library from mRNA isolated from the cells. 10 As described in the above overview, a total of 4,693 sequences expressed by the Km12L4-A cell line were isolated and analyzed; most sequences were about 275-300 nucleotides in length. The KM12L4-A cell line is derived from the KM12C cell line. The KM12C cell line, which is poorly metastatic (low metastatic) was established in culture from a Dukes' stage B₂ surgical specimen (Morikawa et al. Cancer Res. (1988) 48:6863). The KML4-A is 15 a highly metastatic subline derived from KM12C (Yeatman et al. Nucl. Acids. Res. (1995) 23:4007; Bao-Ling et al. Proc. Annu. Meet. Am. Assoc. Cancer. Res. (1995) 21:3269). The KM12C and KM12C-derived cell lines (e.g., KM12L4, KM12L4-A, etc.) are wellrecognized in the art as a model cell line for the study of colon cancer (see, e.g., Moriakawa et al., supra; Radinsky et al. Clin. Cancer Res. (1995) 1:19; Yeatman et al., (1995) supra; 20 Yeatman et al. Clin. Exp. Metastasis (1996) 14:246). The sequences were first masked to eliminate low complexity sequences using the XBLAST masking program (Claverie "Effective Large-Scale Sequence Similarity Searches," In: Computer Methods for Macromolecular Sequence Analysis, Doolittle, ed., Meth. Enzymol. 266:212-227 Academic Press, NY, NY (1996); see particularly Claverie, in "Automated DNA Sequencing and Analysis Techniques" Adams et al., eds., Chap. 36, p. 267 Academic 25 Press, San Diego, 1994 and Claverie et al. Comput. Chem. (1993) 17:191). Generally, masking does not influence the final search results, except to eliminate of relative little interest due to their lox complexity, and to eliminate multiple "hits" based on similarity to repetitive regions common to multiple sequences, e.g., Alu repeats. Masking resulted in the elimination of 43 sequences. The remaining sequences were then used in a BLASTN vs. 30 Genbank search with search parameters of greater than 70% overlap, 99% identity, and a p value of less than 1×10^{-40} , which search resulted in the discarding of 1,432 sequences. Sequences from this search also were discarded if the inclusive parameters were met, but the sequence was ribosomal or vector-derived.

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The resulting sequences from the previous search were classified into three groups (1, 2 and 3 below) and searched in a BLASTX vs. NRP (non-redundant proteins) database search: (1) unknown (no hits in the Genbank search), (2) weak similarity (greater than 45% identity and p value of less than 1×10^{-5}), and (3) high similarity (greater than 60% overlap, greater than 80% identity, and p value less than 1×10^{-5}). This search resulted in discard of 98 sequences as having greater than 70% overlap, greater than 99% identity, and p value of less than 1×10^{-40} .

The remaining sequences were classified as unknown (no hits), weak similarity, and high similarity (parameters as above). Two searches were performed on these sequences. First, a BLAST vs. EST database search resulted in discard of 1771 sequences (sequences with greater than 99% overlap, greater than 99% similarity and a p value of less than 1 x 10⁻⁴⁰; sequences with a p value of less than 1 x 10⁻⁶⁵ when compared to a database sequence of human origin were also excluded). Second, a BLASTN vs. Patent GeneSeq database resulted in discard of 15 sequences (greater than 99% identity; p value less than 1 x 10⁻⁴⁰; greater than 99% overlap).

The remaining sequences were subjected to screening using other rules and redundancies in the dataset. Sequences with a p value of less than 1 x 10⁻¹¹¹ in relation to a database sequence of human origin were specifically excluded. The final result provided the 404 sequences listed in the accompanying Sequence Listing. The Sequence Listing is arranged beginning with sequences with no similarity to any sequence in a database searched, and ending with sequences with the greatest similarity. Each identified polynucleotide represents sequence from at least a partial mRNA transcript. Polynucleotides that were determined to be novel were assigned a sequence identification number.

The novel polynucleotides and were assigned sequence identification numbers SEQ ID NOS: 1-404. The DNA sequences corresponding to the novel polynucleotides are provided in the Sequence Listing. The majority of the sequences are presented in the Sequence Listing in the 5' to 3' direction. A small number, 25, are listed in the Sequence Listing in the 5' to 3' direction but the sequence as written is actually 3' to 5'. These sequences are readily identified with the designation "AR" in the Sequence Name in Table 1 (inserted before the claims). The sequences correctly listed in the 5' to 3' direction in the Sequence Listing are designated "AF." The Sequence Listing filed herewith therefore contains 25 sequences listed in the reverse order, namely SEQ ID NOS:47, 97, 137, 171, 173, 179, 182, 194, 200, 202, 213, 227, 258, 264, 275, 302, 313, 324, 329, 330, 331, 338, 358, 379, and 404.

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Because the provided polynucleotides represent partial mRNA transcripts, two or more polynucleotides of the invention may represent different regions of the same mRNA transcript and the same gene. Thus, if two or more SEQ ID NOS: are identified as belonging to the same clone, then either sequence can be used to obtain the full-length mRNA or gene.

In order to confirm the sequences of SEQ ID NOS:1-404, inserts of the clones corresponding to these polynucleotides were re-sequenced. These "validation" sequences are provided in SEQ ID NOS:405-800. These validation sequences were often longer than the original polynucleotide sequences. They validate, and thus often provide additional sequence information. Validation sequences can be correlated with the original sequences they validate by identifying those sequences of SEQ ID NOS:1-404 and the validation sequences of SEQ ID NOS:405-800 that share the same clone name in Table 1.

Example 2: Results of Public Database Search to Identify Function of Gene Products

SEQ ID NOS:1-404, as well as the validation sequences SEQ ID NOS:405-800, were translated in all three reading frames to determine the best alignment with the individual sequences. These amino acid sequences and nucleotide sequences are referred, generally, as query sequences, which are aligned with the individual sequences. Query and individual sequences were aligned using the BLAST programs, available over the world wide web at http://www.ncbi.nlm.nih.gov/BLAST/. Again the sequences were masked to various extents to prevent searching of repetitive sequences or poly-A sequences, using the XBLAST program for masking low complexity as described above in Example 1.

Table 2 (inserted before the claims) shows the results of the alignments. Table 2 refers to each sequence by its SEQ ID NO:, the accession numbers and descriptions of nearest neighbors from the Genbank and Non-Redundant Protein searches, and the p values of the search results. Table 1 identifies each SEQ ID NO: by SEQ name, clone ID, and cluster. As discussed above, a single cluster includes polynucleotides representing the same gene or gene family, and generally represents sequences encoding the same gene product.

For each of SEQ ID NOS:1-800, the best alignment to a protein or DNA sequence is included in Table 2. The activity of the polypeptide encoded by SEQ ID NOS:1-800 is the same or similar to the nearest neighbor reported in Table 2. The accession number of the nearest neighbor is reported, providing a reference to the activities exhibited by the nearest neighbor. The search program and database used for the alignment also are indicated as well as a calculation of the p value.

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Full length sequences or fragments of the polynucleotide sequences of the nearest neighbors can be used as probes and primers to identify and isolate the full length sequence of SEQ ID NOS:1-800. The nearest neighbors can indicate a tissue or cell type to be used to construct a library for the full-length sequences of SEQ ID NOS:1-800.

SEQ ID NOS:1-800 and the translations thereof may be human homologs of known genes of other species or novel allelic variants of known human genes. In such cases, these new human sequences are suitable as diagnostics or therapeutics. As diagnostics, the human sequences SEQ ID NOS:1-800 exhibit greater specificity in detecting and differentiating human cell lines and types than homologs of other species. The human polypeptides encoded by SEQ ID NOS:1-800 are likely to be less immunogenic when administered to humans than homologs from other species. Further, on administration to humans, the polypeptides encoded by SEQ ID NOS:1-800 can show greater specificity or can be better regulated by other human proteins than are homologs from other species.

15 Example 3: Members of Protein Families

After conducting a profile search as described in the specification above, several of the polynucleotides of the invention were found to encode polypeptides having characteristics of a polypeptide belonging to a known protein families (and thus represent new members of these protein families) and/or comprising a known functional domain (Table 3). Thus the invention encompasses fragments, fusions, and variants of such polynucleotides that retain biological activity associated with the protein family and/or functional domain identified herein.

Table 3 Polynucleotides encoding gene products of a protein family or having a known functional domain(s).

SEQ ID NO:	Biological Activity (Profile hit)	Start	Stop	Dir
24	4 transmembrane segments integral membrane proteins	1218	578	rev
41	4 transmembrane segments integral membrane proteins	1086	413	rev
101	4 transmembrane segments integral membrane proteins	1206	544	rev
157	4 transmembrane segments integral membrane proteins	721	33	rev
341	4 transmembrane segments integral membrane proteins	1253	613	rev
395	4 transmembrane segments integral membrane proteins	530	10	for
395	4 transmembrane segments integral membrane proteins	696	17	for
395	4 transmembrane segments integral membrane proteins	471	39	rev
24	7 transmembrane receptor (Secretin family)	1301	491	rev
41	7 transmembrane receptor (Secretin family)	1309	10	rev
101	7 transmembrane receptor (Secretin family)	1330	296	rev
157	7 transmembrane receptor (Secretin family)	1173	249	rev
291	7 transmembrane receptor (Secretin family)	1400	269	rev

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 Table 3 Polynucleotides encoding gene products of a protein family or having a known functional domain(s).

SEQ ID	Biological Activity (Profile hit)	Start	Ston	Dir
NO:	Diological Activity (1 rollie mit)	Start	Stop	יווען
291	7 transmembrane receptor (Secretin family)	712	130	for
305	7 transmembrane receptor (Secretin family)	926	4	for
305	7 transmembrane receptor (Secretin family)	753	55	rev
315	7 transmembrane receptor (Secretin family)	1058	270	rev
341	7 transmembrane receptor (Secretin family)	1265	534	rev
116	Ank repeat	141	218	for
251	Ank repeat	290	207	for
251	Ank repeat	467	387	for
63	ATPases Associated with Various Cellular Activities	543	60	for
116	ATPases Associated with Various Cellular Activities	802	313	for
134	ATPases Associated with Various Cellular Activities	525	57	rev
136	ATPases Associated with Various Cellular Activities	712	163	for
151	ATPases Associated with Various Cellular Activities	719	73	for
151	ATPases Associated with Various Cellular Activities	386	13	for
384	ATPases Associated with Various Cellular Activities	664	140	for
404	ATPases Associated with Various Cellular Activities	704	52	for
374	Basic region plus leucine zipper transcription factors	298	146	for
97	Bromodomain (conserved sequence found in human,	230	63	for
	Drosophila and yeast proteins.)			
136	EF-hand	121	207	for
242	EF-hand	238	155	for
379	EF-hand	212	126	for
308	Eukaryotic aspartyl proteases	1300	461	rev
213	GATA family of transcription factors	720	377	for
367	G-protein alpha subunit	971	467	rev
188	Phorbol esters/diacylglycerol binding	91	177	for
251	Phorbol esters/diacylglycerol binding	133	219	for
202	protein kinase	482	1	rev
202	protein kinase	970	1	rev
315	protein kinase	739	158	for
315	protein kinase	1023	197	for
367	protein kinase	1046	285	rev
397	protein kinase	511	6	for
256	Protein phosphatase 2C	13	90	for
256	Protein phosphatase 2C	163	86	for
382	Protein Tyrosine Phosphatase	261	2	for
306	SH3 Domain	141	296	for
386	SH3 Domain	359	209	for
169	Trypsin	764	164	rev
188	WD domain, G-beta repeats	480	382	for
188	WD domain, G-beta repeats	206	117	for
335	WD domain, G-beta repeats	3	92	for
23	wnt family of developmental signaling proteins	1151	335	rev
291	wnt family of developmental signaling proteins	779	89	rev
291	wnt family of developmental signaling proteins	1347	382	rev
324	wnt family of developmental signaling proteins	1180	499	rev
330	wnt family of developmental signaling proteins	1180	499	rev
341	wnt family of developmental signaling proteins	1399	560	rev

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Table 3 Polynucleotides encoding gene products of a protein family or having a known functional domain(s).

SEQ ID	Biological Activity (Profile hit)	Start	Stop	Dir
NO:		1	1	1
353	wnt family of developmental signaling proteins	880	49	rev
188	WW/rsp5/WWP domain containing proteins	431	354	for
379	WW/rsp5/WWP domain containing proteins	12	89	for
395	WW/rsp5/WWP domain containing proteins	153	76	for
395	WW/rsp5/WWP domain containing proteins	156	64	for
61	Zinc finger, C2H2 type	254	192	for
306	Zinc finger, C2H2 type	428	367	for
386	Zinc finger, C2H2 type	191	253	for
322	Zinc finger, CCHC class	553	503	for
306	Zinc-binding metalloprotease domain	101	60	rev
395	Zinc-binding metalloprotease domain	28	69	rev

Start and stop indicate the position within the individual sequenes that align with the query sequence having the indicated SEQ ID NO. The direction (Dir) indicates the orientation of the query sequence with respect to the individual sequence, where forward (for) indicates that the alignment is in the same direction (left to right) as the sequence provided in the Sequence Listing and reverse (rev) indicates that the alignment is with a sequence complementary to the sequence provided in the Sequence Listing.

Some polynucleotides exhibited multiple profile hits because, for example, the particular sequence contains overlapping profile regions, and/or the sequence contains two different functional domains. These profile hits are described in more detail below.

a) Four Transmembrane Integral Membrane Proteins. SEQ ID NOS: 24, 41, 101, 157, 341, and 395 correspond to a sequence encoding a polypeptide that is a member of the 4 transmembrane segments integral membrane protein family (transmembrane 4 family). The transmembrane 4 family of proteins includes a number of evolutionarily-related eukaryotic cell surface antigens (Levy et al., J. Biol. Chem., (1991) 266:14597; Tomlinson et al., Eur. J. Immunol. (1993) 23:136; Barclay et al. The leucocyte antigen factbooks. (1993) Academic Press, London/San Diego). The proteins belonging to this family include: 1) Mammalian antigen CD9 (MIC3), which is involved in platelet activation and aggregation; 2)

Mammalian leukocyte antigen CD37, expressed on B lymphocytes; 3) Mammalian leukocyte antigen CD53 (OX-44), which is implicated in growth regulation in hematopoietic cells; 4) Mammalian lysosomal membrane protein CD63 (melanoma-associated antigen ME491; antigen AD1); 5) Mammalian antigen CD81 (cell surface protein TAPA-1), which is implicated in regulation of lymphoma cell growth; 6) Mammalian antigen CD82 (protein

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R2; antigen C33; Kangai 1 (KAI1)), which associates with CD4 or CD8 and delivers costimulatory signals for the TCR/CD3 pathway; 7) Mammalian antigen CD151 (SFA-1; platelet-endothelial tetraspan antigen 3 (PETA-3)); 8) Mammalian cell surface glycoprotein A15 (TALLA-1; MXS1); 9) Mammalian novel antigen 2 (NAG-2); 10) Human tumorassociated antigen CO-029; 11) Schistosoma mansoni and japonicum 23 Kd surface antigen (SM23 / SJ23).

The members of the 4 transmembrane family share several characteristics. First, they all are apparently type III membrane proteins, which are integral membrane proteins containing an N-terminal membrane-anchoring domain which is not cleaved during

10 biosynthesis and which functions both as a translocation signal and as a membrane anchor. The family members also contain three additional transmembrane regions, at least seven conserved cysteines residues, and are of approximately the same size (218 to 284 residues). These proteins are collectively know as the "transmembrane 4 superfamily" (TM4) because they span plasma membrane four times. A schematic diagram of the domain structure of these proteins is as follows:

- where Cyt is the cytoplasmic domain, TMa is the transmembrane anchor; TM2 to TM4 represents transmembrane regions 2 to 4, 'C' are conserved cysteines, and '* 'indicates the position of the consensus pattern. The consensus pattern spans a conserved region including two cysteines located in a short cytoplasmic loop between two transmembrane domains:

 Consensus pattern: G-x(3)-[LIVMF]-x(2)-[GSA]-[LIVMF](2)-G-C-x-[GA]-[STA]- x(2)-[EG]-x(2)-[CWN]-[LIVM](2).
 - b) Seven Transmembrane Integral Membrane Proteins. SEQ ID NOS: 24, 41, 101, 157, 291, 305, 315, and 341 correspond to a sequence encoding a polypeptide that is a member of the seven transmembrane receptor family. G-protein coupled receptors (Strosberg, Eur. J. Biochem. (1991) 196:1; Kerlavage, Curr. Opin. Struct. Biol. (1991) 1:394; and Probst et al., DNA Cell Biol. (1992) 11:1; and Savarese et al., Biochem. J. (1992)
- 30 1:394; and Probst et al., DNA Cell Biol. (1992) 11:1; and Savarese et al., Biochem. J. (1992 293:1) (also called R7G) are an extensive group of hormones, neurotransmitters, odorants and light receptors which transduce extracellular signals by interaction with guanine nucleotide-binding (G) proteins. The tertiary structure of these receptors is thought to be highly similar. They have seven hydrophobic regions, each of which most probably spans

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the membrane. The N-terminus is located on the extracellular side of the membrane and is often glycosylated, while the C-terminus is cytoplasmic and generally phosphorylated. Three extracellular loops alternate with three intracellular loops to link the seven transmembrane regions. Most, but not all of these receptors, lack a signal peptide. The most conserved parts of these proteins are the transmembrane regions and the first two cytoplasmic loops. A conserved acidic-Arg-aromatic triplet is present in the N-terminal extremity of the second cytoplasmic loop (Attwood *et al.*, *Gene* (1991) *98*:153) and could be implicated in the interaction with G proteins.

To detect this widespread family of proteins a pattern is used that contains the conserved triplet and that also spans the major part of the third transmembrane helix. Additional information about the seven transmembrane receptor family, and methods for their identification and use, is found in U.S. Patent No. 5,759,804. Due in part to their expression on the cell surface and other attractive characteristics, seven transmembrane protein family members are of particular interest as drug targets, as surface antigen markers, and as drug delivery targets (*e.g.*, using antibody-drug complexes and/or use of anti-seven transmembrane protein antibodies as therapeutics in their own right).

c) Ank Repeats. SEQ ID NOS: 116 and 251 represent polynucleotides encoding Ank repeat-containing proteins. The ankyrin motif is a 33 amino acid sequence named after the protein ankyrin which has 24 tandem 33-amino-acid motifs. Ank repeats were originally identified in the cell-cycle-control protein cdc10 (Breeden *et al.*, *Nature* (1987) 329:651). Proteins containing ankyrin repeats include ankyrin, myotropin, I-kappaB proteins, cell cycle protein cdc10, the Notch receptor (Matsuno *et al.*, *Development* (1997) 124(21):4265); G9a (or BAT8) of the class III region of the major histocompatibility complex (Biochem J. 290:811-818, 1993), FABP, GABP, 53BP2, Lin12, glp-1, SW14, and SW16. The functions of the ankyrin repeats are compatible with a role in protein-protein interactions (Bork, *Proteins* (1993) 17(4):363; Lambert and Bennet, *Eur. J. Biochem.* (1993) 211:1; Kerr *et al.*, *Current Op. Cell Biol.* (1992) 4:496; Bennet *et al.*, *J. Biol. Chem.* (1980) 255:6424).

The 90 kD N-terminal domain of ankyrin contains a series of 24 33-amino-acid ank repeats. (Lux *et al.*, *Nature* (1990) *344*:36-42, Lambert *et al.*, *PNAS USA* (1990) *87*:1730.)

The 24 ank repeats form four folded subdomains of 6 repeats each. These four repeat subdomains mediate interactions with at least 7 different families of membrane proteins. Ankyrin contains two separate binding sites for anion exchanger dimers. One site utilizes repeat subdomain two (repeats 7-12) and the other requires both repeat subdomains 3 and 4 (repeats 13-24). Since the anion exchangers exist in dimers, ankyrin binds 4 anion

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wo 99/33982 PCT/US98/27610 exchangers at the same time. (Michaely and Bennett, *J. Biol. Chem.* (1995) 270(37):22050) The repeat motifs are involved in ankyrin interaction with tubulin, spectrin, and other membrane proteins. (Lux *et al.*, *Nature* (1990) 344:36.)

The Rel/NF-kappaB/Dorsal family of transcription factors have activity that is controlled by sequestration in the cytoplasm in association with inhibitory proteins referred to as I-kappaB. (Gilmore, Cell (1990) 62:841; Nolan and Baltimore, Curr Opin Genet Dev. (1992) 2:211; Baeuerle, Biochim Biophys Acta (1991) 1072:63; Schmitz et al., Trends Cell Biol. (1991) 1:130.) I-kappaB proteins contain 5 to 8 copies of 33 amino acid ankyrin repeats and certain NF-kappaB/rel proteins are also regulated by cis-acting ankyrin repeat containing domains including p105NF-kappaB which contains a series of ankyrin repeats (Diehl and Hannink, J. Virol. (1993) 67(12):7161). The I-kappaBs and Cactus (also containing ankyrin repeats) inhibit activators through differential interactions with the Relhomology domain. The gene family includes proto-oncogenes, thus broadly implicating IkappaB in the control of both normal gene expression and the aberrant gene expression that makes cells cancerous. (Nolan and Baltimore, Curr Opin Genet Dev. (1992) 2(2):211-220). In the case of rel/NF-kappaB and pp40/I-kappaBβ, both the ankyrin repeats and the carboxyterminal domain are required for inhibiting DNA-binding activity and direct association of pp40/I-kappaBβ with rel/NF-kappaB protein. The ankyrin repeats and the carboxy-terminal of pp40/I-kappaBβ (form a structure that associates with the rel homology domain to inhibit DNA binding activity (Inoue et al., PNAS USA (1992) 89:4333).

The 4 ankyrin repeats in the amino terminus of the transcription factor subunit GABPβ are required for its interaction with the GABPα subunit to form a functional high affinity DNA-binding protein. These repeats can be crosslinked to DNA when GABP is bound to its target sequence. (Thompson *et al.*, *Science* (1991) 253:762; LaMarco *et al.*, *Science* (1991) 253:789).

Myotrophin, a 12.5 kDa protein having a key role in the initiation of cardiac hypertrophy, comprises ankyrin repeats. The ankyrin repeats are characteristic of a hairpin-like protruding tip followed by a helix-turn-helix motif. The V-shaped helix-turn-helix of the repeats stack sequentially in bundles and are stabilized by compact hydrophobic cores, whereas the protruding tips are less ordered.

d) <u>ATPases Associated with Various Cellular Activities (AAA).</u> SEQ ID NOS: 63, 116, 134, 136, 151, 384, and 404 polynucleotides encoding novel members of the "ATPases Associated with diverse cellular Activities" (AAA) protein family The AAA protein family

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is composed of a large number of ATPases that share a conserved region of about 220 amino acids that contains an ATP-binding site (Froehlich *et al.*, *J. Cell Biol.* (1991) 114:443; Erdmann *et al. Cell* (1991) 64:499; Peters *et al.*, EMBO J. (1990) 9:1757; Kunau *et al.*, Biochimie (1993) 75:209-224; Confalonieri *et al.*, BioEssays (1995) 17:639;

http://yeamob.pci.chemie.uni-tuebingen.de/AAA/Description.html). The proteins that belong to this family either contain one or two AAA domains.

Proteins containing two AAA domains include: 1) Mammalian and drosophila NSF (N-ethylmaleimide-sensitive fusion protein) and the fungal homolog, SEC18, which are involved in intracellular transport between the endoplasmic reticulum and Golgi, as well as between different Golgi cisternae; 2) Mammalian transitional endoplasmic reticulum ATPase (previously known as p97 or VCP), which is involved in the transfer of membranes from the endoplasmic reticulum to the golgi apparatus. This ATPase forms a ring-shaped homooligomer composed of six subunits. The yeast homolog, CDC48, plays a role in spindle pole proliferation; 3) Yeast protein PAS1 essential for peroxisome assembly and the related protein PAS1 from Pichia pastoris; 4) Yeast protein AFG2; 5) Sulfolobus acidocaldarius protein SAV and Halobacterium salinarium cdcH, which may be part of a transduction pathway connecting light to cell division.

Proteins containing a single AAA domain include: 1) Escherichia coli and other bacteria ftsH (or hflB) protein. FtsH is an ATP-dependent zinc metallopeptidase that 20 degrades the heat-shock sigma-32 factor, and is an integral membrane protein with a large cytoplasmic C-terminal domain that contain both the AAA and the protease domains; 2) Yeast protein YME1, a protein important for maintaining the integrity of the mitochondrial compartment. YME1 is also a zinc-dependent protease; 3) Yeast protein AFG3 (or YTA10). This protein also contains an AAA domain followed by a zinc-dependent protease domain; 25 4) Subunits from regulatory complex of the 26S proteasome (Hilt et al., Trends Biochem. Sci. (1996) 21:96), which is involved in the ATP-dependent degradation of ubiquitinated proteins, which subunits include: a) Mammalian 4 and homologs in other higher eukaryotes, in yeast (gene YTA5) and fission yeast (gene mts2); b) Mammalian 6 (TBP7) and homologs in other higher eukaryotes and in yeast (gene YTA2); c) Mammalian subunit 7 (MSS1) and 30 homologs in other higher eukaryotes and in yeast (gene CIM5 or YTA3); d) Mammalian subunit 8 (P45) and homologs in other higher eukaryotes and in yeast (SUG1 or CIM3 or TBY1) and fission yeast (gene let1); e) Other probable subunits include human TBP1, which influences HIV gene expression by interacting with the virus tat transactivator protein, and yeast YTA1 and YTA6; 5) Yeast protein BCS1, a mitochondrial protein essential for the

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expression of the Rieske iron-sulfur protein; 6) Yeast protein MSP1, a protein involved in intramitochondrial sorting of proteins; 7) Yeast protein PAS8, and the corresponding proteins PAS5 from Pichia pastoris and PAY4 from Yarrowia lipolytica; 8) Mouse protein SKD1 and its fission yeast homolog (SpAC2G11.06); 9) Caenorhabditis elegans meiotic spindle formation protein mei-1; 10) Yeast protein SAP1' 11) Yeast protein YTA7; and 12) Mycobacterium leprae hypothetical protein A2126A.

In general, the AAA domains in these proteins act as ATP-dependent protein clamps(Confalonieri *et al.* (1995) *BioEssays 17*:639). In addition to the ATP-binding 'A' and 'B' motifs, which are located in the N-terminal half of this domain, there is a highly conserved region located in the central part of the domain which was used in the development of the signature pattern. The consensus pattern is: [LIVMT]-x-[LIVMT]-[LIVMF]-x-[GATMC]-[ST]-[NS]-x(4)-[LIVM]- D-x-A-[LIFA]-x-R.

e) <u>Basic Region Plus Leucine Zipper Transcription Factors.</u> SEQ ID NO:374 correspond to a polynucleotide encoding a novel member of the family of basic region plus leucine zipper transcription factors. The bZIP superfamily (Hurst, *Protein Prof.* (1995) 2:105; and Ellenberger, *Curr. Opin. Struct. Biol.* (1994) 4:12) of eukaryotic DNA-binding transcription factors encompasses proteins that contain a basic region mediating sequence-specific DNA-binding followed by a leucine zipper required for dimerization. Members of the family include transcription factor AP-1, which binds selectively to enhancer elements in the cis control regions of SV40 and metallothionein IIA. AP-1, also known as c-jun, is the cellular homolog of the avian sarcoma virus 17 (ASV17) oncogene v-jun.

Other members of this protein family include jun-B and jun-D, probable transcription factors that are highly similar to jun/AP-1; the fos protein, a proto-oncogene that forms a non-covalent dimer with c-jun; the fos-related proteins fra-1, and fos B; and mammalian cAMP response element (CRE) binding proteins CREB, CREM, ATF-1, ATF-3, ATF-4, ATF-5, ATF-6 and LRF-1. The consensus pattern for this protein family is: [KR]-x(1,3)-[RKSAQ]-N-x(2)-[SAQ](2)-x-[RKTAENQ]-x-R-x-[RK].

f) <u>Bromodomain.</u> SEQ ID NO:97 corresponds to a polynucleotide encoding a polypeptide having a bromodomain region (Haynes et al., 1992, Nucleic Acids Res. 20:2693-2603, Tamkun et al., 1992, Cell 68:561-572, and Tamkun, 1995, Curr. Opin. Genet. Dev. 5:473-477), which is a conserved region of about 70 amino acids found in the following proteins: 1) Higher eukaryotes transcription initiation factor TFIID 250 Kd subunit (TBP-associated factor p250) (gene CCG1); P250 is associated with the TFIID TATA-box binding protein and seems essential for progression of the G1 phase of the cell

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wo 99/33982 PCT/US98/27610 cycle. 2) Human RING3, a protein of unknown function encoded in the MHC class II locus; 3) Mammalian CREB-binding protein (CBP), which mediates cAMP-gene regulation by binding specifically to phosphorylated CREB protein; 4) Mammalian homologs of brahma, including three brahma-like human: SNF2a(hBRM), SNF2b, and BRG1; 5) Human BS69, a protein that binds to adenovirus E1A and inhibits E1A transactivation; 6) Human peregrin (or Br140).

The bromodomain is thought to be involved in protein-protein interactions and may be important for the assembly or activity of multicomponent complexes involved in transcriptional activation. The consensus pattern, which spans a major part of the bromodomain, is: [STANVF]-x(2)-F-x(4)-[DNS]-x(5,7)-[DENQTF]-Y-[HFY]-x(2)-[LIVMFY]-x(3)-[LIVM]-x(4)-[LIVM]-x(6,8)-Y-x(12,13)-[LIVM]-x(2)-N-[SACF]-x(2)-[FY].

g) <u>EF-Hand.</u> SEQ ID NOS:136, 242, and 379 correspond to polynucleotides encoding a novel protein in the family of EF-hand proteins. Many calcium-binding proteins belong to the same evolutionary family and share a type of calcium-binding domain known as the EF-hand (Kawasaki *et al.*, *Protein. Prof.* (1995) 2:305-490). This type of domain consists of a twelve residue loop flanked on both sides by a twelve residue alpha-helical domain. In an EF-hand loop the calcium ion is coordinated in a pentagonal bipyramidal configuration. The six residues involved in the binding are in positions 1, 3, 5, 7, 9 and 12; these residues are denoted by X, Y, Z, -Y, -X and -Z. The invariant Glu or Asp at position 12 provides two oxygens for liganding Ca (bidentate ligand).

Proteins known to contain EF-hand regions include: Calmodulin (Ca=4, except in yeast where Ca=3) ("Ca=" indicates approximate number of EF-hand regions); diacylglycerol kinase (EC 2.7.1.107) (DGK) (Ca=2); 2) FAD-dependent glycerol-3-phosphate dehydrogenase (EC 1.1.99.5) from mammals (Ca=1); guanylate cyclase activating protein (GCAP) (Ca=3); MIF related proteins 8 (MRP-8 or CFAG) and 14 (MRP-14) (Ca=2); myosin regulatory light chains (Ca=1); oncomodulin (Ca=2); osteonectin (basement membrane protein BM-40) (SPARC); and proteins that contain an "osteonectin" domain (QR1, matrix glycoprotein SC1).

The consensus pattern includes the complete EF-hand loop as well as the first residue which follows the loop and which seem to always be hydrophobic.

Consensus pattern: D-x-[DNS]-{ILVFYW}-[DENSTG]-[DNQGHRK]-{GP}-[LIVMC]-[DENQSTAGC]-x(2)-[DE]-[LIVMFYW]

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h) Eukaryotic Aspartyl Proteases. SEQ ID NO:308 corresponds to a gene encoding a novel eukaryotic aspartyl protease. Aspartyl proteases, known as acid proteases, (EC 3.4.23.-) are a widely distributed family of proteolytic enzymes (Foltmann B., Essays Biochem. (1981) 17:52; Davies D.R., Annu. Rev. Biophys. Chem. (1990) 19:189; Rao J.K.M., et al., Biochemistry (1991) 30:4663) known to exist in vertebrates, fungi, plants, 5 retroviruses and some plant viruses. Aspartate proteases of eukaryotes are monomeric enzymes which consist of two domains. Each domain contains an active site centered on a catalytic aspartyl residue. The two domains most probably evolved from the duplication of an ancestral gene encoding a primordial domain. Currently known eukaryotic aspartyl proteases include: 1) Vertebrate gastric pepsins A and C (also known as gastricsin); 2) 10 Vertebrate chymosin (rennin), involved in digestion and used for making cheese; 3) Vertebrate lysosomal cathepsins D (EC 3.4.23.5) and E (EC 3.4.23.34); 4) Mammalian renin (EC 3.4.23.15) whose function is to generate angiotensin I from angiotensinogen in the plasma; 5) Fungal proteases such as aspergillopepsin A (EC 3.4.23.18), candidapepsin (EC 3.4.23.24), mucoropepsin (EC 3.4.23.23) (mucor rennin), endothiapepsin (EC 3.4.23.22), 15 polyporopepsin (EC 3.4.23.29), and rhizopuspepsin (EC 3.4.23.21); and 6) Yeast saccharopepsin (EC 3.4.23.25) (proteinase A) (gene PEP4). PEP4 is implicated in posttranslational regulation of vacuolar hydrolases; 7) Yeast barrierpepsin (EC 3.4.23.35) (gene BAR1); a protease that cleaves alpha-factor and thus acts as an antagonist of the 20 mating pheromone; and 8) Fission yeast sxal which is involved in degrading or processing the mating pheromones.

Most retroviruses and some plant viruses, such as badnaviruses, encode for an aspartyl protease which is an homodimer of a chain of about 95 to 125 amino acids. In most retroviruses, the protease is encoded as a segment of a polyprotein which is cleaved during the maturation process of the virus. It is generally part of the pol polyprotein and, more rarely, of the gag polyprotein. Because the sequence around the two aspartates of eukaryotic aspartyl proteases and around the single active site of the viral proteases is conserved, a single signature pattern can be used to identify members of both groups of proteases. The consensus pattern is: [LIVMFGAC]-[LIVMTADN]-[LIVFSA]-D-[ST]-G-[STAV]-[STAPDENQ]- x-[LIVMFSTNC]-x-[LIVMFGTA], where D is the active site residue.

i) <u>GATA Family of Transcription Factors.</u> SEQ ID NO:213 corresponds to a novel member of the GATA family of transcription factors. The GATA family of transcription factors are proteins that bind to DNA sites with the consensus sequence (A/T)GATA(A/G), found within the regulatory region of a number of genes. Proteins currently known to belong

WO 99/33982 PCT/US98/27610 to this family are: 1) GATA-1 (Trainor, C.D., et al., Nature (1990) 343:92) (also known as Eryfl, GF-1 or NF-E1), which binds to the GATA region of globin genes and other genes expressed in erythroid cells. It is a transcriptional activator which probably serves as a general 'switch' factor for erythroid development; 2) GATA-2 (Lee, M.E., et al., J. Biol. Chem. (1991) 266:16188), a transcriptional activator which regulates endothelin-1 gene 5 expression in endothelial cells; 3) GATA-3 (Ho, I.-C., et al., EMBO J. (1991) 10:1187), a transcriptional activator which binds to the enhancer of the T-cell receptor alpha and delta genes; 4) GATA-4 (Spieth, J., et al., Mol. Cell. Biol. (1991) 11:4651), a transcriptional activator expressed in endodermally derived tissues and heart; 5) Drosophila protein pannier 10 (or DGATAa) (gene pnr) which acts as a repressor of the achaete-scute complex (as-c); 6) Bombyx mori BCFI (Drevet, J.R., et al., J. Biol. Chem. (1994) 269:10660), which regulates the expression of chorion genes; 7) Caenorhabditis elegans elt-1 and elt-2, transcriptional activators of genes containing the GATA region, including vitellogenin genes (Hawkins, M.G., et al., J. Biol. Chem. (1995) 270:14666); 8) Ustilago may dis urbs1 (Voisard, C.P.O., 15 et al., Mol. Cell. Biol. (1993) 13:7091), a protein involved in the repression of the biosynthesis of siderophores; 9) Fission yeast protein GAF2.

All these transcription factors contain a pair of highly similar 'zinc finger' type domains with the consensus sequence C-x2-C-x17-C-x2-C. Some other proteins contain a single zinc finger motif highly related to those of the GATA transcription factors. These 20 proteins are: 1) Drosophila box A-binding factor (ABF) (also known as protein serpent (gene srp)) which may function as a transcriptional activator protein and may play a key role in the organogenesis of the fat body; 2) Emericella nidulans are (Arst, H.N., Jr., et al., Trends Genet. (1989) 5:291) a transcriptional activator which mediates nitrogen metabolite repression; 3) Neurospora crassa nit-2 (Fu, Y.-H., et al., Mol. Cell. Biol. (1990) 10:1056), a 25 transcriptional activator which turns on the expression of genes coding for enzymes required for the use of a variety of secondary nitrogen sources, during conditions of nitrogen limitation; 4) Neurospora crassa white collar proteins 1 and 2 (WC-1 and WC-2), which control expression of light-regulated genes; 5) Saccharomyces cerevisiae DAL81 (or UGA43), a negative nitrogen regulatory protein; 6) Saccharomyces cerevisiae GLN3, a 30 positive nitrogen regulatory protein; 7) Saccharomyces cerevisiae GAT1; 8) Saccharomyces cerevisiae GZF3.

The consensus pattern for the GATA family is: C-x-[DN]-C-x(4,5)-[ST]-x(2)-W-[HR]-[RK]-x(3)-[GN]-x(3,4)-C-N-[AS]-C, where the four C's are zinc ligands.

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j) <u>G-Protein Alpha Subunit</u>. SEQ ID NO:367 corresponds to a gene encoding a novel polypeptide of the G-protein alpha subunit family. Guanine nucleotide binding proteins (G-proteins) are a family of membrane-associated proteins that couple extracellularly-activated integral-membrane receptors to intracellular effectors, such as ion channels and enzymes that vary the concentration of second messenger molecules. G-proteins are composed of 3 subunits (alpha, beta and gamma) which, in the resting state, associate as a trimer at the inner face of the plasma membrane. The alpha subunit has a molecule of guanosine diphosphate (GDP) bound to it. Stimulation of the G-protein by an activated receptor leads to its exchange for GTP (guanosine triphosphate). This results in the separation of the alpha from the beta and gamma subunits, which always remain tightly associated as a dimer. Both the alpha and beta-gamma subunits are then able to interact with effectors, either individually or in a cooperative manner. The intrinsic GTPase activity of the alpha subunit hydrolyses the bound GTP to GDP. This returns the alpha subunit to its inactive conformation and allows it to reassociate with the beta-gamma subunit, thus restoring the system to its resting state.

G-protein alpha subunits are 350-400 amino acids in length and have molecular weights in the range 40-45 kDa. Seventeen distinct types of alpha subunit have been identified in mammals. These fall into 4 main groups on the basis of both sequence similarity and function: alpha-s, alpha-q, alpha-i and alpha-12 (Simon *et al.*, *Science* (1993) 252:802). Many alpha subunits are substrates for ADP-ribosylation by cholera or pertussis toxins. They are often N-terminally acylated, usually with myristate and/or palmitoylate, and these fatty acid modifications are probably important for membrane association and high- affinity interactions with other proteins. The atomic structure of the alpha subunit of the G-protein involved in mammalian vision, transducin, has been elucidated in both GTP- and GDB-bound forms, and shows considerable similarity in both primary and tertiary structure in the nucleotide-binding regions to other guanine nucleotide binding proteins, such as p21-ras and EF-Tu.

k) <u>Phorbol Esters/Diacylglycerol Binding.</u> SEQ ID NO:188 and 251 represent polynucleotides encoding a protein belonging to the family including phorbol esters/diacylglycerol binding proteins. Diacylglycerol (DAG) is an important second messenger. Phorbol esters (PE) are analogues of DAG and potent tumor promoters that cause a variety of physiological changes when administered to both cells and tissues. DAG activates a family of serine/threonine protein kinases, collectively known as protein kinase C (PKC) (Azzi *et al.*, *Eur. J. Biochem.* (1992) 208:547). Phorbol esters can directly stimulate PKC. The N-terminal region of PKC, known as C1, has been shown (Ono *et al.*, *Proc. Natl.*

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Acad. Sci. USA (1989) 86:4868) to bind PE and DAG in a phospholipid and zinc-dependent fashion. The C1 region contains one or two copies (depending on the isozyme of PKC) of a cysteine-rich domain about 50 amino-acid residues long and essential for DAG/PE-binding. Such a domain has also been found in, for example, the following proteins.

- (1) Diacylglycerol kinase (EC 2.7.1.107) (DGK) (Sakane *et al.*, *Nature* (1990) 344:345), the enzyme that converts DAG into phosphatidate. It contains two copies of the DAG/PE-binding domain in its N-terminal section. At least five different forms of DGK are known in mammals; and
- (2) N-chimaerin, a brain specific protein which shows sequence similarities with the BCR protein at its C-terminal part and contains a single copy of the DAG/PE-binding domain at its N-terminal part. It has been shown (Ahmed *et al.*, *Biochem. J.* (1990) 272:767, and Ahmed *et al.*, *Biochem. J.* (1991) 280:233) to be able to bind phorbol esters.

The DAG/PE-binding domain binds two zinc ions; the ligands of these metal ions are probably the six cysteines and two histidines that are conserved in this domain. The signature pattern completely spans the DAG/PE domain. The consensus pattern is: H-x-[LIVMFYW]-x(8,11)-C-x(2)-C-x(3)-[LIVMFC]-x(5,10)-C-x(2)-C-x(4)-[HD]-x(2)-C-x(5,9)-C. All the C and H are probably involved in binding zinc.

1) Protein Kinase. SEQ ID NOS:202, 315, 367, and 397 represent polynucleotides encoding protein kinases. Protein kinases catalyze phosphorylation of proteins in a variety of pathways, and are implicated in cancer. Eukaryotic protein kinases (Hanks S.K., et al., FASEB J. (1995) 9:576; Hunter T., Meth. Enzymol. (1991) 200:3; Hanks S.K., et al., Meth. Enzymol. (1991) 200:38; Hanks S.K., Curr. Opin. Struct. Biol. (1991) 1:369; Hanks S.K., et al., Science (1988) 241:42) are enzymes that belong to a very extensive family of proteins which share a conserved catalytic core common to both serine/threonine and tyrosine protein kinases. There are a number of conserved regions in the catalytic domain of protein kinases. Two of the conserved regions are the basis for the signature pattern in the protein kinase profile. The first region, which is located in the N-terminal extremity of the catalytic domain, is a glycine-rich stretch of residues in the vicinity of a lysine residue, which has been shown to be involved in ATP binding. The second region, which is located in the central part of the catalytic domain, contains a conserved aspartic acid residue which is important for the catalytic activity of the enzyme (Knighton D.R., et al., Science (1991) 253:407). The protein kinase profile includes two signature patterns for this second region: one specific for serine/threonine kinases and the other for tyrosine kinases. A third profile is

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based on the alignment in (Hanks S.K., et al., FASEB J. (1995) 9:576) and covers the entire catalytic domain. The consensus patterns are as follows:

- 1) Consensus pattern: [LIV]-G-{P}-G-{P}-[FYWMGSTNH]-[SGA]-{PW}-[LIVCAT]-{PD}-x-[GSTACLIVMFY]-x(5,18)-[LIVMFYWCSTAR]-[AIVP]-
- [LIVMFAGCKR]-K, where K binds ATP. The majority of known protein kinases are detected by this pattern. Proteins kinases that are not detected by this consensus include viral kinases, which are quite divergent in this region and are completely missed by this pattern.
- 2) Consensus pattern: [LIVMFYC]-x-[HY]-x-D-[LIVMFY]-K-x(2)-N-[LIVMFYCT](3), where D is an active site residue. This consensus sequence identifies most serine/threonine-specific protein kinases with only 10 exceptions. Half of the exceptions are viral kinases, while the other exceptions include Epstein-Barr virus BGLF4 and Drosophila ninaC, which have Ser and Arg, respectively, instead of the conserved Lys. These latter two protein kinases are detected by the tyrosine kinase specific pattern described below.
 - 3) Consensus pattern: [LIVMFYC]-x-[HY]-x-D-[LIVMFY]-[RSTAC]-x(2)-N-[LIVMFYC], where D is an active site residue. All tyrosine-specific protein kinases are detected by this consensus pattern, with the exception of human ERBB3 and mouse blk. This pattern also detects most bacterial aminoglycoside phosphotransferases (Benner S., *Nature* (1987) 329:21; Kirby R., *J. Mol. Evol.* (1992) 30:489) and herpesviruses ganciclovir kinases (Littler E., *et al.*, *Nature* (1992) 358:160), which are structurally and evolutionary related to protein kinases.

The protein kinase profile also detects receptor guanylate cyclases and 2-5A-dependent ribonucleases. Sequence similarities between these two families and the eukaryotic protein kinase family have been noticed previously. The profile also detects Arabidopsis thaliana kinase-like protein TMKL1 which seems to have lost its catalytic activity.

If a protein analyzed includes the two of the above protein kinase signatures, the probability of it being a protein kinase is close to 100%. Eukaryotic-type protein kinases have also been found in prokaryotes such as Myxococcus xanthus (Munoz-Dorado J., *et al.*, *Cell* (1991) 67:995) and Yersinia pseudotuberculosis. The patterns shown above has been updated since their publication in (Bairoch A., *et al.*, *Nature* (1988) 331:22).

m) <u>Protein Phosphatase 2C</u>, SEQ ID NO:256 corresponds to a polynucleotide encoding a novel protein phosphatase 2C (PP2C), which is one of the four major classes of mammalian serine/threonine specific protein phosphatases. PP2C (Wenk *et al.*, *FEBS Lett*.

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WO 99/33982 PCT/US98/27610 (1992) 297:135) is a monomeric enzyme of about 42 Kd which shows broad substrate specificity and is dependent on divalent cations (mainly manganese and magnesium) for its activity. Three isozymes are currently known in mammals: PP2C-alpha, -beta and -gamma.

n) Protein Tyrosine Phosphatase. SEQ ID NO:382 represents a polynucleotide encoding a protein tyrosine kinase. Tyrosine specific protein phosphatases (EC 3.1.3.48) (PTPase) (Fischer et al., Science (1991) 253:401; Charbonneau et al., Annu. Rev. Cell Biol. (1992) 8:463; Trowbridge, J. Biol. Chem. (1991) 266:23517; Tonks et al., Trends Biochem. Sci. (1989) 14:497; and Hunter, Cell (1989) 58:1013) catalyze the removal of a phosphate group attached to a tyrosine residue. These enzymes are very important in the control of cell growth, proliferation, differentiation and transformation. Multiple forms of PTPase have been characterized and can be classified into two categories: soluble PTPases and transmembrane receptor proteins that contain PTPase domain(s).

Soluble PTPases include PTPN3 (H1) and PTPN4 (MEG), enzymes that contain an N-terminal band 4.1-like domain and could act at junctions between the membrane and cytoskeleton; PTPN6 (PTP-1C; HCP; SHP) and PTPN11 (PTP-2C; SH-PTP3; Syp), enzymes that contain two copies of the SH2 domain at its N-terminal extremity.

Dual specificity PTPases include DUSP1 (PTPN10; MAP kinase phosphatase-1; MKP-1) which dephosphorylates MAP kinase on both Thr-183 and Tyr-185; and DUSP2 (PAC-1), a nuclear enzyme that dephosphorylates MAP kinases ERK1 and ERK2 on both Thr and Tyr residues.

Structurally, all known receptor PTPases are made up of a variable length extracellular domain, followed by a transmembrane region and a C-terminal catalytic cytoplasmic domain. Some of the receptor PTPases contain fibronectin type III (FN-III) repeats, immunoglobulin-like domains, MAM domains or carbonic anhydrase-like domains in their extracellular region. The cytoplasmic region generally contains two copies of the PTPAse domain. The first seems to have enzymatic activity, while the second is inactive but seems to affect substrate specificity of the first. In these domains, the catalytic cysteine is generally conserved but some other, presumably important, residues are not.

PTPase domains consist of about 300 amino acids. There are two conserved cysteines and the second one has been shown to be absolutely required for activity. Furthermore, a number of conserved residues in its immediate vicinity have also been shown to be important. The consensus pattern for PTPases is: [LIVMF]-H-C-x(2)-G-x(3)-[STC]-[STAGP]-x-[LIVMFY]; C is the active site residue.

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o) SH3 Domain. SEQ ID NO:306 and 386 represent polynucleotides encoding SH3 domain proteins. The Src homology 3 (SH3) domain is a small protein domain of about 60 amino acid residues first identified as a conserved sequence in the non-catalytic part of several cytoplasmic protein tyrosine kinases (e.g. Src, Abl, Lck) (Mayer *et al.*, *Nature* (1988) 332:272). The domain has also been found in a variety of intracellular or membrane-associated proteins (Musacchio *et al.*, *FEBS Lett.* (1992) 307:55; Pawson *et al.*, *Curr. Biol.* (1993) 3:434; Mayer *et al.*, *Trends Cell Biol.* (1993) 3:8; and Pawson *et al.*, *Nature* (1995) 373:573).

The SH3 domain has a characteristic fold that consists of five or six beta-strands arranged as two tightly packed anti-parallel beta sheets. The linker regions may contain short helices (Kuriyan *et al.*, *Curr. Opin. Struct. Biol.* (1993) 3:828). It is believed that SH3 domain-containing proteins mediate assembly of specific protein complexes via binding to proline-rich peptides (Morton *et al.*, *Curr. Biol.* (1994) 4:615). In general, SH3 domains are found as single copies in a given protein, but there is a significant number of proteins with two SH3 domains and a few with 3 or 4 copies.

SH3 domains have been identified in, for example, protein tyrosine kinases, such as the Src, Abl, Bkt, Csk and ZAP70 families of kinases; mammalian phosphatidylinositol-specific phospholipase C-gamma-1 and -2; mammalian phosphatidyl inositol 3-kinase regulatory p85 subunit; mammalian Ras GTPase-activating protein (GAP); mammalian Vav oncoprotein, a guanine nucleotide exchange factor of the CDC24 family; Drosophila lethal(1)discs large-1 tumor suppressor protein (gene Dlg1); mammalian tight junction protein ZO-1; vertebrate erythrocyte membrane protein p55; Caenorhabditis elegans protein lin-2; rat protein CASK; and mammalian synaptic proteins SAP90/PSD-95, CHAPSYN-110/PSD-93, SAP97/DLG1 and SAP102. Novel SH3-domain containing polypeptides will facilitate elucidation of the role of such proteins in important biological pathways, such as ras activation.

p) <u>Trypsin</u>. SEQ ID NO:169 corresponds to a novel serine protease of the trypsin family. The catalytic activity of the serine proteases from the trypsin family is provided by a charge relay system involving an aspartic acid residue hydrogen-bonded to a histidine, which itself is hydrogen-bonded to a serine. The sequences in the vicinity of the active site serine and histidine residues are well conserved in this family of proteases (Brenner S., *Nature* (1988) *334*:528). Proteases known to belong to the trypsin family include: 1) Acrosin; 2) Blood coagulation factors VII, IX, X, XI and XII, thrombin, plasminogen, and protein C; 3) Cathepsin G; 4) Chymotrypsins; 5) Complement components C1r, C1s, C2, and complement

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WO 99/33982 PCT/US98/27610 factors B, D and I; 6) Complement-activating component of RA-reactive factor; 7) Cytotoxic cell proteases (granzymes A to H); 8) Duodenase I; 9) Elastases 1, 2, 3A, 3B (protease E), leukocyte (medullasin).; 10) Enterokinase (EC 3.4.21.9) (enteropeptidase); 11) Hepatocyte growth factor activator; 12) Hepsin; 13) Glandular (tissue) kallikreins (including EGFbinding protein types A, B, and C, NGF-gamma chain, gamma-renin, prostate specific antigen (PSA) and tonin); 14) Plasma kallikrein; 15) Mast cell proteases (MCP) 1 (chymase) to 8; 16) Myeloblastin (proteinase 3) (Wegener's autoantigen); 17) Plasminogen activators (urokinase-type, and tissue-type); 18) Trypsins I, II, III, and IV; 19) Tryptases; 20) Snake venom proteases such as ancrod, batroxobin, cerastobin, flavoxobin, and protein C activator; 21) Collagenase from common cattle grub and collagenolytic protease from Atlantic sand fiddler crab; 22) Apolipoprotein(a); 23) Blood fluke cercarial protease; 24) Drosophila trypsin like proteases: alpha, easter, snake-locus; 25) Drosophila protease stubble (gene sb); and 26) Major mite fecal allergen Der p III. All the above proteins belong to family S1 in the classification of peptidases (Rawlings N.D., et al., Meth. Enzymol. (1994) 244:19; http://www.expasy.ch/cgi-bin/lists?peptidas.txt) and originate from eukaryotic species. It

The consensus patterns for this trypsin protein family are: 1) [LIVM]-[ST]-A-[STAG]-H-C, where H is the active site residue. All sequences known to belong to this class detected by the pattern, except for complement components C1r and C1s, pig plasminogen, bovine protein C, rodent urokinase, ancrod, gyroxin and two insect trypsins; 2) [DNSTAGC]-[GSTAPIMVQH]-x(2)-G-[DE]-S-G-[GS]-[SAPHV]- [LIVMFYWH]- [LIVMFYSTANQH], where S is the active site residue. All sequences known to belong to this family are detected by the above consensus sequences, except for 18 different proteases which have lost the first conserved glycine. If a protein includes both the serine and the histidine active site signatures, the probability of it being a trypsin family serine protease is 100%.

should be noted that bacterial proteases that belong to family S2A are similar enough in the

regions of the active site residues that they can be picked up by the same patterns.

q) <u>WD Domain, G-Beta Repeats.</u> SEQ ID NOS:188 and 335 represent novel members of the WD domain/G-beta repeat family. Beta-transducin (G-beta) is one of the three subunits (alpha, beta, and gamma) of the guanine nucleotide-binding proteins (G proteins) which act as intermediaries in the transduction of signals generated by transmembrane receptors (Gilman, *Annu. Rev. Biochem.* (1987) 56:615). The alpha subunit binds to and hydrolyzes GTP; the functions of the beta and gamma subunits are less clear but

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they seem to be required for the replacement of GDP by GTP as well as for membrane anchoring and receptor recognition.

In higher eukaryotes, G-beta exists as a small multigene family of highly conserved proteins of about 340 amino acid residues. Structurally, G-beta consists of eight tandem repeats of about 40 residues, each containing a central Trp-Asp motif (this type of repeat is sometimes called a WD-40 repeat). Such a repetitive segment has been shown to exist in a number of other proteins including: human LIS1, a neuronal protein involved in type-1 lissencephaly; and mammalian coatomer beta' subunit (beta'-COP), a component of a cytosolic protein complex that reversibly associates with Golgi membranes to form vesicles that mediate biosynthetic protein transport.

The consensus pattern for the WD domain/G-Beta repeat family is: [LIVMSTAC]-[LIVMFYWSTAGC]-[LIVMSTAG]-[LIVMSTAGC]-x(2)-[DN]-x(2)-[LIVMWSTAC]-x-[LIVMFSTAG]-W-[DEN]-[LIVMFSTAGCN].

r) wnt Family of Developmental Signaling Proteins. SEQ ID NO: 23, 291, 324, 330, 15 341, and 353 correspond to novel members of the wnt family of developmental signaling proteins. Wnt-1 (previously known as int-1), the seminal member of this family, (Nusse R., Trends Genet. (1988) 4:291) is a proto-oncogene induced by the integration of the mouse mammary tumor virus. It is thought to play a role in intercellular communication and seems to be a signalling molecule important in the development of the central nervous system 20 (CNS). The sequence of wnt-1 is highly conserved in mammals, fish, and amphibians. Wnt-1 was found to be a member of a large family of related proteins (Nusse R., et al., Cell (1992) 69:1073; McMahon A.P., Trends Genet. (1992) 8:1; Moon R.T., BioEssays (1993) 15:91) that are all thought to be developmental regulators. These proteins are known as wnt-2 (also known as irp), wnt-3, -3A, -4, -5A, -5B, -6, -7A, -7B, -8, -8B, -9 and -10. At least 25 four members of this family are present in Drosophila; one of them, wingless (wg), is implicated in segmentation polarity. All these proteins share the following features characteristics of secretory proteins: a signal peptide, several potential N-glycosylation sites and 22 conserved cysteines that are probably involved in disulfide bonds. The Wnt proteins seem to adhere to the plasma membrane of the secreting cells and are therefore likely to 30 signal over only few cell diameters. The consensus pattern, which is based upon a highly conserved region including three cysteines, is as follows: C-K-C-H-G-[LIVMT]-S-G-x-C. All sequences known to belong to this family are detected by the provided consensus pattern.

s) <u>Ww/rsp5/WWP Domain-Containing Proteins.</u> SEQ ID NOS:188, 379, and 395 represent polynucleotides encoding a polypeptide in the family of WW/rsp5/WWP domain-

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containing proteins. The WW domain (Bork et al., Trends Biochem. Sci. (1994) 19:531; Andre et al., Biochem. Biophys. Res. Commun. (1994) 205:1201; Hofmann et al., FEBS Lett. (1995) 358:153; and Sudol et al., FEBS Lett. (1995) 369:67), also known as rsp5 or WWP), was originally discovered as a short conserved region in a number of unrelated proteins, among them dystrophin, the gene responsible for Duchenne muscular dystrophy. The domain, which spans about 35 residues, is repeated up to 4 times in some proteins. It has been shown (Chen et al., Proc. Natl. Acad. Sci. USA (1995) 92:7819) to bind proteins with particular proline-motifs, [AP]-P-P-[AP]-Y, and thus resembles somewhat SH3 domains. It appears to contain beta-strands grouped around four conserved aromatic positions, generally Trp. The name WW or WWP derives from the presence of these Trp as well as that of a conserved Pro. It is frequently associated with other domains typical for proteins in signal transduction processes.

Proteins containing the WW domain include:

- Dystrophin, a multidomain cytoskeletal protein. Its longest alternatively
 spliced form consists of an N-terminal actin-binding domain, followed by 24 spectrin-like repeats, a cysteine-rich calcium-binding domain and a C-terminal globular domain.
 Dystrophins form tetramers and is thought to have multiple functions including involvement in membrane stability, transduction of contractile forces to the extracellular environment and organization of membrane specialization. Mutations in the dystrophin gene lead to muscular dystrophy of Duchenne or Becker type. Dystrophin contains one WW domain C-terminal of the spectrin-repeats.
 - 2. Vertebrate YAP protein, which is a substrate of an unknown serine kinase. It binds to the SH3 domain of the Yes oncoprotein via a proline-rich region. This protein appears in alternatively spliced isoforms, containing either one or two WW domains.
 - 3. IQGAP, which is a human GTPase activating protein acting on ras. It contains an N-terminal domain similar to fly muscle mp20 protein and a C-terminal ras GTPase activator domain.

For the sensitive detection of WW domains, the profile spans the whole homology region as well as a pattern. The consensus for this family is: W-x(9,11)-[VFY]-[FYW]-x(6,7)-[GSTNE]-[GSTQCR]-[FYW]-x(2)-P.

t) Zinc Finger, C2H2 Type. SEQ ID NO:61, 306, and 386 correspond to polynucleotides encoding novel members of the of the C2H2 type zinc finger protein family. Zinc finger domains (Klug et al., Trends Biochem. Sci. (1987) 12:464; Evans et al., Cell (1988) 52:1; Payre et al., FEBS Lett. (1988) 234:245; Miller et al., EMBO J. (1985) 4:1609;

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wo 99/33982 PCT/US98/27610 and Berg, *Proc. Natl. Acad. Sci. USA* (1988) 85:99) are nucleic acid-binding protein structures first identified in the Xenopus transcription factor TFIIIA. These domains have since been found in numerous nucleic acid-binding proteins. A zinc finger domain is composed of 25 to 30 amino acid residues. Two cysteine or histidine residues are positioned at both extremities of the domain, which are involved in the tetrahedral coordination of a zinc atom. It has been proposed that such a domain interacts with about five nucleotides.

Many classes of zinc fingers are characterized according to the number and positions of the histidine and cysteine residues involved in the zinc atom coordination. In the first class to be characterized, called C2H2, the first pair of zinc coordinating residues are cysteines, while the second pair are histidines. A number of experimental reports have demonstrated the zinc-dependent DNA or RNA binding property of some members of this class.

Mammalian proteins having a C2H2 zipper include (number in parenthesis indicates number of zinc finger regions in the protein): basonuclin (6), BCL-6/LAZ-3 (6), erythroid krueppel-like transcription factor (3), transcription factors Sp1 (3), Sp2 (3), Sp3 (3) and Sp(4) 3, transcriptional repressor YY1 (4), Wilms' tumor protein (4), EGR1/Krox24 (3), EGR2/Krox20 (3), EGR3/Pilot (3), EGR4/AT133 (4), Evi-1 (10), GLI1 (5), GLI2 (4+), GLI3 (3+), HIV-EP1/ZNF40 (4), HIV-EP2 (2), KR1 (9+), KR2 (9), KR3 (15+), KR4 (14+), KR5 (11+), HF.12 (6+), REX-1 (4), ZfX (13), ZfY (13), Zfp-35 (18), ZNF7 (15), ZNF8 (7), ZNF35 (10), ZNF42/MZF-1 (13), ZNF43 (22), ZNF46/Kup (2), ZNF76 (7), ZNF91 (36), ZNF133 (3).

In addition to the conserved zinc ligand residues, it has been shown that a number of other positions are also important for the structural integrity of the C2H2 zinc fingers. (Rosenfeld *et al.*, *J. Biomol. Struct. Dyn.* (1993) 11:557) The best conserved position is found four residues after the second cysteine; it is generally an aromatic or aliphatic residue.

The consensus pattern for C2H2 zinc fingers is: C-x(2,4)-C-x(3)-[LIVMFYWC]-x(8)-H-x(3,5)-H. The two C's and two H's are zinc ligands.

u) Zinc Finger, CCHC Class. SEQ ID NO:322 corresponds to a polynucleotide encoding a novel member of the zinc finger CCHC family. The CCHC zinc finger protein family to date has been mostly composed of retroviral gag proteins (nucleocapsid). The prototype structure of this family is from HIV. The family also contains members involved in eukaryotic gene regulation, such as C. elegans GLH-1. The consensus sequence of this family is based upon the common structure of an 18-residue zinc finger.

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v) Zinc-Binding Metalloprotease Domain. SEQ ID NO:306 and 395 represent polynucleotides encoding novel members of the zinc-binding metalloprotease domain protein family. The majority of zinc-dependent metallopeptidases (with the notable exception of the carboxypeptidases) share a common pattern of primary structure (Jongeneel et al., FEBS Lett. (1989) 242:211; Murphy et al., FEBS Lett. (1991) 289:4; and Bode et al., 5 Zoology (1996) 99:237) in the part of their sequence involved in the binding of zinc, and can be grouped together as a superfamily, known as the metzincins, on the basis of this sequence similarity. Examples of these proteins include: 1) Angiotensin-converting enzyme (EC 3.4.15.1) (dipeptidyl carboxypeptidase I) (ACE), the enzyme responsible for hydrolyzing angiotensin I to angiotensin II. 2) Mammalian extracellular matrix metalloproteinases 10 (known as matrixins) (Woessner, FASEB J. (1991) 5:2145): MMP-1 (EC 3.4.24.7) (interstitial collagenase), MMP-2 (EC 3.4.24.24) (72 Kd gelatinase), MMP-9 (EC 3.4.24.35) (92 Kd gelatinase), MMP-7 (EC 3.4.24.23) (matrylisin), MMP-8 (EC 3.4.24.34) (neutrophil collagenase), MMP-3 (EC 3.4.24.17) (stromelysin-1), MMP-10 (EC 3.4.24.22) 15 (stromelysin-2), and MMP-11 (stromelysin-3), MMP-12 (EC 3.4.24.65) (macrophage metalloelastase). 3) Endothelin-converting enzyme 1 (EC 3.4.24.71) (ECE-1), which processes the precursor of endothelin to release the active peptide.

A signature pattern which includes the two histidine and the glutamic acid residues is sufficient to detect this superfamily of proteins, having the consensus pattern: [GSTALIVN]-x(2)-H-E-[LIVMFYW]-{DEHRKP}-H-x-[LIVMFYWGSPQ]. The two H's are zinc ligands, and E is the active site residue.

Example 4: Differential Expression of Polynucleotides of the Invention: Description of Libraries and Detection of Differential Expression

The relative expression levels of the polynucleotides of the invention was assessed in several libraries prepared from various sources, including cell lines and patient tissue samples. Table 4 provides a summary of these libraries, including the shortened library name (used hereafter), the mRNA source used to prepared the cDNA library, the "nickname" of the library that is used in the tables below (in quotes), and the approximate number of clones in the library.

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Table 4 Description of cDNA Libraries

Library (lib #)	Description	Number of Clones in this
(110 11)		Clustering
1	Km12 L4 Human Colon Cell Line, High Metastatic Potential (derived from Km12C) "High Colon"	307133
2	Km12C Human Colon Cell Line, Low Metastatic Potential "Low Colon"	284755
3	MDA-MB-231 Human Breast Cancer Cell Line, High Metastatic Potential; micro-metastases in lung "High Breast"	326937
4	MCF7 Human Breast Cancer Cell, Non Metastatic "Low Breast"	318979
8	MV-522 Human Lung Cancer Cell Line, High Metastatic Potential "High Lung"	223620
9	UCP-3 Human Lung Cancer Cell Line, Low Metastatic Potential "Low Lung"	312503
12	Human microvascular endothelial cells (HMEC) – Untreated PCR (OligodT) cDNA library	41938
13	Human microvascular endothelial cells (HMEC) – bFGF treated PCR (OligodT) cDNA library	42100
14	Human microvascular endothelial cells (HMEC) – VEGF treated PCR (OligodT) cDNA library	42825
15	Normal Colon – UC#2 Patient PCR (OligodT) cDNA library "Normal Colon Tumor Tissue"	34285
16	Colon Tumor – UC#2 Patient PCR (OligodT) cDNA library "Normal Colon Tumor Tissue"	35625
17	Liver Metastasis from Colon Tumor of UC#2 Patient PCR (OligodT) cDNA library "High Colon Metastasis Tissue"	36984
18	Normal Colon – UC#3 Patient PCR (OligodT) cDNA library "Normal Colon Tumor Tissue"	36216
19	Colon Tumor – UC#3 Patient PCR (OligodT) cDNA library "High Colon Tumor Tissue"	41388
20	Liver Metastasis from Colon Tumor of UC#3 Patient PCR (OligodT) cDNA library "High Colon Metastasis Tissue"	30956

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The KM12L4 and KM12C cell lines are described in Example 1 above. The MDA-MB-231 cell line was originally isolated from pleural effusions (Cailleau, J. Natl. Cancer. Inst. (1974) 53:661), is of high metastatic potential, and forms poorly differentiated adenocarcinoma grade II in nude mice consistent with breast carcinoma. The MCF7 cell line 5 was derived from a pleural effusion of a breast adenocarcinoma and is non-metastatic. The MV-522 cell line is derived from a human lung carcinoma and is of high metastatic potential. The UCP-3 cell line is a low metastatic human lung carcinoma cell line; the MV-522 is a high metastatic variant of UCP-3. These cell lines are well-recognized in the art as models for the study of human breast and lung cancer (see, e.g., Chandrasekaran et al., Cancer Res. (1979) 39:870 (MDA-MB-231 and MCF-7); Gastpar et al., J Med Chem (1998) 10 41:4965 (MDA-MB-231 and MCF-7); Ranson et al., Br J Cancer (1998) 77:1586 (MDA-MB-231 and MCF-7); Kuang et al., Nucleic Acids Res (1998) 26:1116 (MDA-MB-231 and MCF-7); Varki et al., Int J Cancer (1987) 40:46 (UCP-3); Varki et al., Tumour Biol. (1990) 11:327; (MV-522 and UCP-3); Varki et al., Anticancer Res. (1990) 10:637; (MV-522); 15 Kelner et al., Anticancer Res (1995) 15:867 (MV-522); and Zhang et al., Anticancer Drugs (1997) 8:696 (MV522)). The samples of libraries 15-20 are derived from two different patients (UC#2, and UC#3).

Each of the libraries is composed of a collection of cDNA clones that in turn are representative of the mRNAs expressed in the indicated mRNA source. In order to facilitate the analysis of the millions of sequences in each library, the sequences were assigned to clusters. The concept of "cluster of clones" is derived from a sorting/grouping of cDNA clones based on their hybridization pattern to a panel of roughly 300 7bp oligonucleotide probes (see Drmanac et al., Genomics (1996) 37(1):29). Random cDNA clones from a tissue library are hybridized at moderate stringency to 300 7bp oligonucleotides. Each oligonucleotide has some measure of specific hybridization to that specific clone. The combination of 300 of these measures of hybridization for 300 probes equals the "hybridization signature" for a specific clone. Clones with similar sequence will have similar hybridization signatures. By developing a sorting/grouping algorithm to analyze these signatures, groups of clones in a library can be identified and brought together computationally. These groups of clones are termed "clusters". Depending on the stringency of the selection in the algorithm (similar to the stringency of hybridization in a classic library cDNA screening protocol), the "purity" of each cluster can be controlled. For example, artifacts of clustering may occur in computational clustering just as artifacts can occur in "wet-lab" screening of a cDNA library with 400 bp cDNA fragments, at even the

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highest stringency. The stringency used in the implementation of cluster herein provides groups of clones that are in general from the same cDNA or closely related cDNAs. Closely related clones can be a result of different length clones of the same cDNA, closely related clones from highly related gene families, or splice variants of the same cDNA.

Differential expression for a selected cluster was assessed by first determining the number of cDNA clones corresponding to the selected cluster in the first library (Clones in 1st), and the determining the number of cDNA clones corresponding to the selected cluster in the second library (Clones in 2nd). Differential expression of the selected cluster in the first library relative to the second library is expressed as a "ratio" of percent expression between the two libraries. In general, the "ratio" is calculated by: 1) calculating the percent expression of the selected cluster in the first library by dividing the number of clones corresponding to a selected cluster in the first library by the total number of clones analyzed from the first library; 2) calculating the percent expression of the selected cluster in the second library by dividing the number of clones corresponding to a selected cluster in a second library by the total number of clones analyzed from the second library; 3) dividing the calculated percent expression from the first library by the calculated percent expression from the second library. If the "number of clones" corresponding to a selected cluster in a library is zero, the value is set at 1 to aid in calculation. The formula used in calculating the ratio takes into account the "depth" of each of the libraries being compared, i.e., the total number of clones analyzed in each library.

In general, a polynucleotide is said to be significantly differentially expressed between two samples when the ratio value is greater than at least about 2, preferably greater than at least about 3, more preferably greater than at least about 5, where the ratio value is calculated using the method described above. The significance of differential expression is determined using a z score test (Zar, <u>Biostatistical Analysis</u>, Prentice Hall, Inc., USA, "Differences between Proportions," pp 296-298 (1974).

Tables 5 to 7 (inserted before the claims) show the number of clones in each of the above libraries that were analyzed for differential expression. Examples of differentially expressed polynucleotides of particular interest are described in more detail below.

Example 5: Polynucleotides Differentially Expressed in High Metastatic Potential Breast Cancer Cells Versus Low Metastatic Breast Cancer Cells

A number of polynucleotide sequences have been identified that are differentially expressed between cells derived from high metastatic potential breast cancer tissue and low

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metastatic breast cancer cells. Expression of these sequences in breast cancer can be valuable in determining diagnostic, prognostic and/or treatment information. For example, sequences that are highly expressed in the high metastatic potential cells can be indicative of increased expression of genes or regulatory sequences involved in the metastatic process. A patient sample displaying an increased level of one or more of these polynucleotides may thus warrant more aggressive treatment. In another example, sequences that display higher expression in the low metastatic potential cells can be associated with genes or regulatory sequences that inhibit metastasis, and thus the expression of these polynucleotides in a sample may warrant a more positive prognosis than the gross pathology would suggest.

The differential expression of these polynucleotides can be used as a diagnostic marker, a prognostic marker, for risk assessment, patient treatment and the like. These polynucleotide sequences can also be used in combination with other known molecular and/or biochemical markers.

The following table summarizes identified polynucleotides with differential expression between high metastatic potential breast cancer cells and low metastatic potential breast cancer cells.

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 Table 8.
 Differentially expressed polynucleotides: High metastatic potential breast cancer vs. low metastatic breast cancer cells

SEQ ID	Differential Expression	Cluster		Clones in	Ratio
NO.		ID	1 st	2 nd	
			Library	Library	
9	High Breast > Low Breast (Lib3 > Lib4)	2623	31	4	7.561356
42	High Breast > Low Breast (Lib3 > Lib4)	307	196	75	2.549721
52	High Breast > Low Breast (Lib3 > Lib4)	19	1364	525	2.534854
62	High Breast > Low Breast (Lib3 > Lib4)	2623	31	4	7.561356
65	High Breast > Low Breast (Lib3 > Lib4)	5749	9	0	8.780930
66	High Breast > Low Breast (Lib3 > Lib4)	6455	6	0	5.853953
68	High Breast > Low Breast (Lib3 > Lib4)	6455	6	0	5.853953
114	High Breast > Low Breast (Lib3 > Lib4)	2030	32	4	7.805271
123	High Breast > Low Breast (Lib3 > Lib4)	3389	13	2	6.341782
144	High Breast > Low Breast (Lib3 > Lib4)	4623	12	2	5.853953
172	High Breast > Low Breast (Lib3 > Lib4)	102	278	116	2.338217
178	High Breast > Low Breast (Lib3 > Lib4)	3681	10	1	9.756589
214	High Breast > Low Breast (Lib3 > Lib4)	3900	8	1	7.805271
219	High Breast > Low Breast (Lib3 > Lib4)	3389	13	2	6.341782
223	High Breast > Low Breast (Lib3 > Lib4)	1399	19	7	2.648217
258	High Breast > Low Breast (Lib3 > Lib4)	48 37	10	0	9.756589
317	High Breast > Low Breast (Lib3 > Lib4)	1577	25	3	8.130490
379	High Breast > Low Breast (Lib3 > Lib4)	260	27	2	13.17139
4	Low Breast > High Breast (Lib4 > Lib3)	3706	22	4	5.637215
39	Low Breast > High Breast (Lib4 > Lib3)	4016	6	0	6.149690
74	Low Breast > High Breast (Lib4 > Lib3)	6268	18	3	6.149690
81	Low Breast > High Breast (Lib4 > Lib3)	40392	8	1	8.199586
130	Low Breast > High Breast (Lib4 > Lib3)	13183	7	0	7.174638
157	Low Breast > High Breast (Lib4 > Lib3)	5417	9	0	9.224535
162	Low Breast > High Breast (Lib4 > Lib3)	9685	7	0	7.174638
183	Low Breast > High Breast (Lib4 > Lib3)	7337	16	3	5.466391
202	Low Breast > High Breast (Lib4 > Lib3)	6124	9	1	9.224535
298	Low Breast > High Breast (Lib4 > Lib3)	1037	22	4	5.637215
338	Low Breast > High Breast (Lib4 > Lib3)	689	36	17	2.170478
384	Low Breast > High Breast (Lib4 > Lib3)	697	72	30	2.459876
386	Low Breast > High Breast (Lib4 > Lib3)	4568	9	0	9.224535
388	Low Breast > High Breast (Lib4 > Lib3)	5622	13	2	6.662164

5 Example 6: Polynucleotides Differentially Expressed in High Metastatic Potential Lung Cancer Cells Versus Low Metastatic Lung Cancer Cells

A number of polynucleotide sequences have been identified that are differentially expressed between cells derived from high metastatic potential lung cancer tissue and low metastatic lung cancer cells. Expression of these sequences in lung cancer tissue can be valuable in determining diagnostic, prognostic and/or treatment information. For example, sequences that are highly expressed in the high metastatic potential cells are associated can be indicative of increased expression of genes or regulatory sequences involved in the metastatic process. A patient sample displaying an increased level of one or more of these

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polynucleotides may thus warrant more aggressive treatment. In another example, sequences that display higher expression in the low metastatic potential cells can be associated with genes or regulatory sequences that inhibit metastasis, and thus the expression of these polynucleotides in a sample may warrant a more positive prognosis than the gross pathology would suggest.

The differential expression of these polynucleotides can be used as a diagnostic marker, a prognostic marker, for risk assessment, patient treatment and the like. These polynucleotide sequences can also be used in combination with other known molecular and/or biochemical markers.

The following table summarizes identified polynucleotides with differential expression between high metastatic potential lung cancer cells and low metastatic potential lung cancer cells:

Table 9 Differentially expressed polynucleotides: High metastatic potential lung cancer vs. low metastatic lung cancer cells

SEQ ID NO.	Differential Expression	Cluster	Clones in	Clones in 2nd	Ratio
NO.		ID	1 st	-	
400	Web I was I am I was (I il 0 > I il 0)	1.4000	Library	Library	• • • • • • • •
	High Lung > Low Lung (Lib8 > Lib 9)	14929	23	16	2.008868
9	High Lung > Low Lung (Lib8 > Lib9)	2623	6	1	8.384840
34	High Lung > Low Lung (Lib8 > Lib9)	5832	5	0	6.987366
42	High Lung > Low Lung (Lib8 > Lib9)	307	79	27	4.088903
62	High Lung > Low Lung (Lib8 > Lib9)	2623	6	1	8.384840
74	High Lung > Low Lung (Lib8 > Lib9)	6268	5	0	6.987366
106	High Lung > Low Lung (Lib8 > Lib9)	10717	8	Ö	11.17978
119	High Lung > Low Lung (Lib8 > Lib9)	8	1355	122	15.52111
361	High Lung > Low Lung (Lib8 > Lib9)	1120	5	0	6.987366
369	High Lung > Low Lung (Lib8 > Lib9)	2790	6	0	8.384840
371	High Lung > Low Lung (Lib8 > Lib9)	8847	6	1	8.384840
379	High Lung > Low Lung (Lib8 > Lib9)	260	15	0	20.96210
395	High Lung > Low Lung (Lib8 > Lib9)	13538	9	1	12.57726
135	Low Lung > High Lung (Lib9 > Lib8)	36313	30	1	21.46731
154	Low Lung > High Lung (Lib9 > Lib8)	5345	27	6	3.220097
160	Low Lung > High Lung (Lib9 > Lib8)	4386	21	3	5.009039
260	Low Lung > High Lung (Lib9 > Lib8)	4141	27	4	4.830145
308	Low Lung > High Lung (Lib9 > Lib8)	15855	213	12	12.70149
323	Low Lung > High Lung (Lib9 > Lib8)	5257	25	5	3.577885
349	Low Lung > High Lung (Lib9 > Lib8)	2797	14	1	10.01807
381	Low Lung > High Lung (Lib9 > Lib8)	2428	19	2	6.797982

Example 7: Polynucleotides Differentially Expressed in High Metastatic Potential Colon

Cancer Cells Versus Low Metastatic Colon Cancer Cells

A number of polynucleotide sequences have been identified that are differentially expressed between cells derived from high metastatic potential colon cancer tissue and low

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metastatic colon cancer cells. Expression of these sequences in colon cancer tissue can be valuable in determining diagnostic, prognostic and/or treatment information. For example, sequences that are highly expressed in the high metastatic potential cells can be indicative of increased expression of genes or regulatory sequences involved in the metastatic process. A patient sample displaying an increased level of one or more of these polynucleotides may thus warrant more aggressive treatment. In another example, sequences that display higher expression in the low metastatic potential cells can be associated with genes or regulatory sequences that inhibit metastasis, and thus the expression of these polynucleotides in a sample may warrant a more positive prognosis than the gross pathology would suggest.

The differential expression of these polynucleotides can be used as a diagnostic marker, a prognostic marker, for risk assessment, patient treatment and the like. These polynucleotide sequences can also be used in combination with other known molecular and/or biochemical markers.

The following table summarizes identified polynucleotides with differential expression between high metastatic potential colon cancer cells and low metastatic potential colon cancer cells:

Table 11: Differentially expressed polynucleotides: High metastatic potential colon cancer vs. low metastatic colon cancer cells

SEQ ID NO.	Differential Expression	Cluster ID	Clones in 1st	Clones in 2 nd	Ratio
			Library	Library	
1	High Colon > Low Colon (Lib1 > Lib2)	6660	7	0	6.489973
176	High Colon > Low Colon (Lib1 > Lib2)	3765	19	6	2.935940
241	High Colon > Low Colon (Lib1 > Lib2)	4275	11	2	5.099264
362	High Colon > Low Colon (Lib1 > Lib2)	6420	8	0	7.417112
374	High Colon > Low Colon (Lib1 > Lib2)	6420	8	0	7.417112
39	Low Colon > High Colon (Lib2 > Lib1)	4016	14	5	3.020043
97	Low Colon > High Colon (Lib2 > Lib1)	945	21	9	2.516702
134	Low Colon > High Colon (Lib2 > Lib1)	2464	19	5	4.098630
317	Low Colon > High Colon (Lib2 > Lib1)	1577	40	12	3.595289
357	Low Colon > High Colon (Lib2 > Lib1)	4309	13	4	3.505407

20 <u>Example 8:</u> <u>Polynucleotides Differentially Expressed at Higher Levels in High Metastatic</u> <u>Potential Colon Cancer Patient Tissue Versus Normal Patient Tissue</u>

A number of polynucleotide sequences have been identified that are differentially expressed between cells derived from high metastatic potential colon cancer tissue and normal tissue. Expression of these sequences in colon cancer tissue can be valuable in determining diagnostic, prognostic and/or treatment information. For example, sequences that are highly expressed in the high metastatic potential cells are associated can be

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indicative of increased expression of genes or regulatory sequences involved in the advanced disease state which involves processes such as angiogenesis, dedifferentiation, cell replication, and metastasis. A patient sample displaying an increased level of one or more of these polynucleotides may thus warrant more aggressive treatment.

The differential expression of these polynucleotides can be used as a diagnostic marker, a prognostic marker, for risk assessment, patient treatment and the like. These polynucleotide sequences can also be used in combination with other known molecular and/or biochemical markers.

The following table summarizes identified polynucleotides with differential expression between high metastatic potential colon cancer cells and normal colon cells:

Table 11: Differentially expressed polynucleotides: High metastatic potential colon tissue vs. normal colon tissue

SEQ ID NO.	Differential Expression	Cluster ID	Clones in 1 st	Clones in 2 nd	Ratio
			Library	Library	
52	High Colon Metastasis Tissue > Normal Colon Tissue of UC#3 (Lib20 > Lib18)	19	10	0	11.69918
52		19	13	2	6.025646
172	High Colon Metastasis Tissue > Normal Tissue in UC#2 (Lib17 > Lib15)	102	65	22	2.738930

15 Example 9: Polynucleotides Differentially Expressed at Higher Levels in High Colon Tumor Potential Patient Tissue Versus Metastasized Colon Cancer Patient Tissue

A number of polynucleotide sequences have been identified that are differentially expressed between cells derived from high tumor potential colon cancer tissue and cells derived from high metastatic potential colon cancer cells. Expression of these sequences in colon cancer tissue can be valuable in determining diagnostic, prognostic and/or treatment information associated with the transformation of precancerous tissue to malignant tissue. This information can be useful in the prevention of achieving the advanced malignant state in these tissues, and can be important in risk assessment for a patient.

The following table summarizes identified polynucleotides with differential expression between high tumor potential colon cancer tissue and cells derived from high metastatic potential colon cancer cells:

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Table 12: Differentially expressed polynucleotides: High tumor potential colon tissue vs. metastatic colon tissue

SEQ ID	Differential Expression	Cluster	Clones in 1st	Clones in 2 nd	Ratio
NO.		ID	Library	Library	
52	High Colon Tumor Tissue > Metastasis Tissue of UC#3 (Lib19 > Lib20)	19	69	10	5.160829
119	High Colon Tumor Tissue > Metastasis	8	14	1	10.47124
172	Tissue of UC#3 (Lib19 > Lib20) High Colon Tumor Tissue > Metastasis Tissue of UC#3 (Lib19 > Lib20)	102	43	10	3.216168

5 Example 10: Polynucleotides Differentially Expressed at Higher Levels in High Tumor Potential Colon Cancer Patient Tissue Versus Normal Patient Tissue

A number of polynucleotide sequences have been identified that are differentially expressed between cells derived from high tumor potential colon cancer tissue and normal tissue. Expression of these sequences in colon cancer tissue can be valuable in determining diagnostic, prognostic and/or treatment information associated with the prevention of achieving the malignant state in these tissues, and can be important in risk assessment for a patient. For example, sequences that are highly expressed in the potential colon cancer cells are associated with or can be indicative of increased expression of genes or regulatory sequences involved in early tumor progression. A patient sample displaying an increased level of one or more of these polynucleotides may thus warrant closer attention or more frequent screening procedures to catch the malignant state as early as possible.

The following table summarizes identified polynucleotides with differential expression between high metastatic potential colon cancer cells and normal colon cells:

20 **Table 13:** Differentially expressed polynucleotides: High tumor potential colon tissue vs. normal colon tissue

SEQ ID NO.	Differential Expression	Cluster ID	Clones in 1 st Library	Clones in 2 nd Library	Ratio
52	High Colon Tumor Tissue > Normal Tissue of UC#2 (Lib16 > Lib15)	19	13	2	6.255508
288	High Colon Tumor Tissue > Normal Tissue of UC#2 (Lib16 > Lib15)	1267	7	0	6.125253
52	High Colon Tumor Tissue > Normal Tissue of UC#3 (Lib19 > Lib18)	19	69	0	60.37750
119	High Colon Tumor Tissue > Normal Tissue of UC#3 (Lib19 > Lib18)	8	14	1	12.25050
172	High Colon Tumor Tissue > Normal Tissue of UC#3 (Lib19 > Lib18)	102	43	7	5.375222

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Example 11: Polynucleotides Differentially Expressed Across Multiple Libraries

A number of polynucleotide sequences have been identified that are differentially expressed between cancerous cells and normal cells across all three tissue types tested (*i.e.*, breast, colon, and lung). Expression of these sequences in a tissue or any origin can be valuable in determining diagnostic, prognostic and/or treatment information associated with the prevention of achieving the malignant state in these tissues, and can be important in risk assessment for a patient. These polynucleotides can also serve as non-tissue specific markers of, for example, risk of metastasis of a tumor. The following table summarizes identified polynucleotides that were differentially expressed but without tissue typespecificity in the breast, colon, and lung libraries tested.

 Table 14: Polynucleotides Differentially Expressed Across Multiple Library Comparisons

SEQ ID NO.	Differential Expression	Cluster ID	Clones in 1st	Clones in 2 nd	Ratio
			Library	Library	
9	High Breast > Low Breast (Lib3 > Lib4)	2623	31	4	7.561356
	High Lung > Low Lung (Lib8 > Lib9)	2623	6	1	8.384840
39	Low Breast > High Breast (Lib4 > Lib3)	4016	6	0	6.149690
	Low Colon > High Colon (Lib2 > Lib1)	4016	14	5	3.020043
42	High Breast > Low Breast (Lib3 > Lib4)	307	196	75	2.549721
	High Lung > Low Lung (Lib8 > Lib9)	307	79	27	4.088903
52	High Breast > Low Breast (Lib3 > Lib4)	19	1364	525	2.534854
	High Colon Metastasis Tissue > Normal	19	10	0	11.69918
	Colon Tissue of UC#3 (Lib20 > Lib18)				
	High Colon Metastasis Tissue > Normal	19	13	2	6.025646
	Tissue in UC#2 (Lib17 > Lib15)				
	High Colon Tumor Tissue > Metastasis	19	69	10	5.160829
	Tissue of UC#3 (Lib19 > Lib20)				
	High Colon Tumor Tissue > Normal Tissue	19	13	2	6.255508
	of UC#2 (Lib16 > Lib15)				
	High Colon Tumor Tissue > Normal Tissue	19	69	0	60.37750
	of UC#3 (Lib19 > Lib18)				
62	High Breast > Low Breast (Lib3 > Lib4)	2623	31	4	7.561356
	High Lung > Low Lung (Lib8 > Lib9)	2623	6	1	8.384840
74	High Lung > Low Lung (Lib8 > Lib9)	6268	5	0	6.987366
	Low Breast > High Breast (Lib4 > Lib3)	6268	18	3	6.149690
119	High Colon Tumor Tissue > Metastasis	8	14	1	10.47124
	Tissue of UC#3 (Lib19 > Lib20)				
	High Colon Tumor Tissue > Normal Tissue	8	14	1	12.25050
	of UC#3 (Lib19 > Lib18)				
	High Lung > Low Lung (Lib8 > Lib9)	8	1355	122	15.52111
172	High Breast > Low Breast (Lib3 > Lib4)	102	278	116	2.338217
	High Colon Metastasis Tissue > Normal	102	65	22	2.738930
	Tissue in UC#2 (Lib17 > Lib15)				•
	High Colon Tumor Tissue > Metastasis	102	43	10	3.216168
	-				_

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SEQ ID NO.	Differential Expression	Cluster ID	Clones in 1 st Library	Clones in 2 nd Library	Ratio
	Tissue of UC#3 (Lib19 > Lib20) High Colon Tumor Tissue > Normal Tissue of UC#3 (Lib19 > Lib18)	102	43	7	5.375222
317	High Breast > Low Breast (Lib3 > Lib4)	1577	25	3	8.130490
	Low Colon > High Colon (Lib2 > Lib1)	1577	40	12	3.595289
379	High Breast > Low Breast (Lib3 > Lib4)	260	27	2	13.17139
	High Lung > Low Lung (Lib8 > Lib9)	260	15	0	20.96210

Example 12: Polynucleotides Exhibiting Colon-Specific Expression

The cDNA libraries described herein were also analyzed to identify those polynucleotides that were specifically expressed in colon cells or tissue, *i.e.*, the polynucleotides were identified in libraries prepared from colon cell lines or tissue, but not in libraries of breast or lung origin. The polynucleotides that were expressed in a colon cell line and/or in colon tissue, but were present in the breast or lung cDNA libraries described herein, are shown in Table 15.

10 **Table 15** Polynucleotides specifically expressed in colon cells.

SEQ ID	Cluster	Clones in	Clones in	SEQ ID	Cluster	Clones in	Clones in
NO.		1 st Library	^{2nd} Library	NO.		1 st Library	2 nd Library
5	36535	2	0	229	39648	2	0
13	27250	2	0	231	85064	1	0
19	16283	3	0	234	39 391	2	0
24	16918	4	0	236	39498	2	0
26	40108	2	0	242	22113	3	0
32	32663	1	1	247	19255	2	0
43	39833	2	0	252	22814	3	0
47	18957	3	0	253	39563	2	0
48	39508	2	0	254	39420	2	0
56	7005	8	2	257	39412	2	0
58	18957	3	0	261	38085	2	0
59	18957	3	0	265	40054	1	0
60	16283	3	0	266	39423	2	0
64	13238	4	1	267	39453	2	0
70	39442	2	0	270	78091	1	0
71	17036	4	0	276	39168	2	0
73	7005	8	2	277	39458	2	0
83	11476	6	0	278	14391	3	1
86	39425	2	0	279	39195	2	0
94	21847	2	1	282	12977	5	0
100	16731	3	1	284	14391	3	1
101	12439	4	0	290	16347	4	0
113	17055	4	0	293	39478	2	0
120	67907	1	0	294	39392	2	0
121	12081	4	0	297	39180	2	0
124	39174	2	0	299	6867	7	3

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SEQ ID	Cluster	Clones in	Clones in	SEQ ID	Cluster	Clones in	Clones in
NO.			2 nd Library			1 st Library	2 nd Library
126	8210	2	6	301	41633	1	1
128	40455	2	0	302	23218	3	0
139	22195	3	0	303	39380	2	0
143	86859	1	0	309	84328	1	0
150	8672	4	4	314	14367	3	0
153	16977	4	0	320	39886	2	0
156	17036	4	0	324	9061	5	2
159	40044	2	0	327	16653	3	1
161	40044	2	0	328	16985	4	0
163	22155	3	0	329	12977	5	0
166	15066	4	0	330	9061	5	2
170	11465	5	0	333	16392	3	0
176	3765	19	6	342	39486	2	0
181	86110	1	0	344	6874	6	3
182	39648	2	0	345	6874	6	3
185	17076	4	0	353	11494	4	0
186	22794	2	0	354	17062	3	0
187	39171	2	0	355	16245	4	0
194	40455	2	0	356	83103	1	0
199	16317	3	0	358	13072	4	1
210	39186	2	0	366	14364	1	0
211	40122	2	0	368	84182	1	0
218	26295	2	0	372	56020	1	0
222	4665	5	9	389	7514	5	3
226	82498	1	0	391	7570	5	3
227	35702	2	0	393	23210	3	0

In addition to the above, SEQ ID NOS:159 and 161 were each present in one clone in each of Lib16 (Normal Colon Tumor Tissue), and SEQ ID NOS:344 and 345 were each present in one clone in Lib17 (High Colon Metastasis Tissue). No clones corresponding to the colon-specific polynucleotides in the table above were present in any of Libraries 3, 4, 8, or 9. The polynucleotide provided above can be used as markers of cells of colon origin, and find particular use in reference arrays, as described above.

Example 13: Identification of Contiguous Sequences Having a Polynucleotide of the Invention

The novel polynucleotides were used to screen publicly available and proprietary databases to determine if any of the polynucleotides of SEQ ID NOS:1-404 would facilitate identification of a contiguous sequence, *e.g.*, the polynucleotides would provide sequence that would result in 5' extension of another DNA sequence, resulting in production of a longer contiguous sequence composed of the provided polynucleotide and the other DNA sequence(s). Contiging was performed using the AssemblyLign program with the following

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parameters: 1) Overlap: Minimum Overlap Length: 30; % Stringency: 50; Minimum Repeat Length: 30; Alignment: gap creation penalty: 1.00, gap extension penalty: 1.00; 2) Consensus: % Base designation threshold: 80.

Using these parameters, 44 polynucleotides provided contiged sequences. These 5 contiged sequences are provided as SEQ ID NOS:801-844. The contiged sequences can be correlated with the sequences of SEQ ID NOS:1-404 upon which the contiged sequences are based by identifying those sequences of SEQ ID NOS:1-404 and the contiged sequences of SEQ ID NOS:801-844 that share the same clone name in Table 1. It should be noted that of these 44 sequences that provided a contiged sequence, the following members of that group 10 of 44 did not contig using the overlap settings indicated in parentheses (Stringency/Overlap): SEQ ID NO:804 (30%/10); SEQ ID NO:810 (20%/20); SEQ ID NO:812 (30%/10); SEQ ID NO:814 (40%/20); SEQ ID NO:816 (30%/10); SEQ ID NO:832 (30%/10); SEQ ID NO:840 (20%/20); SEQ ID NO:841 (40%/20). To generalize, the indicated polynucleotides did not contig using a minimum 20% stringency, 10 overlap. There was a corresponding increase in 15 the number of degenerate codons in these sequences.

The contiged sequences (SEQ ID NO:801-844) thus represent longer sequences that encompass a polynucleotide sequence of the invention. The contiged sequences were then translated in all three reading frames to determine the best alignment with individual sequences using the BLAST programs as described above for SEO ID NOS:1-404 and the validation sequences SEQ ID NOS:405-800. Again the sequences were masked using the 20 XBLAST profram for masking low complexity as described above in Example 1 (Table 2). Several of the contiged sequences were found to encode polypeptides having characteristics of a polypeptide belonging to a known protein families (and thus represent new members of these protein families) and/or comprising a known functional domain (Table 16). Thus the invention encompasses fragments, fusions, and variants of such polynucleotides that retain biological activity associated with the protein family and/or functional domain identified herein.

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Table 16. Profile hits using contiged sequences

SEQ ID NO.	Sequence Name	Profile	Start (Stop)	Score
809	Contig_RTA00000177AF.n.18.3. Seq_THC123051	ATPases	778 (1612)	6040
824	Contig_RTA00000187AF.g.24.1. Seq_THC168636	homeobox	531 (707)	12080
824	Contig_RTA00000187AF.g.24.1. Seq_THC168636	MAP kinase kinase	769 (1494)	5784
833	Contig_RTA00000190AF.j.4.1. Seq_THC228776	protein kinase	170 (1010)	5027
833	Contig_RTA00000190AF.j.4.1. Seq_THC228776	protein kinase	170 (1010)	5027

All stop/start sequences are provided in the forward direction.

The profiles for the ATPases (AAA) and protein kinase families are described above in Example 2. The homeobox and MAP kinase kinase protein families are described further below.

Homeobox domain. The 'homeobox' is a protein domain of 60 amino acids (Gehring In: Guidebook to the Homeobox Genes, Duboule D., Ed., pp1-10, Oxford University Press, Oxford, (1994); Buerglin In: Guidebook to the Homeobox Genes, pp25-72, Oxford University Press, Oxford, (1994); Gehring Trends Biochem. Sci. (1992) 17:277-280; Gehring et al Annu. Rev. Genet. (1986) 20:147-173; Schofield Trends Neurosci. (1987) 10:3-6; http://copan.bioz.unibas.ch/ homeo.html) first identified in number of Drosophila homeotic and segmentation proteins. It is extremely well conserved in many other animals, including vertebrates. This domain binds DNA through a helix-turn-helix type of structure. Several proteins that contain a homeobox domain play an important role in development. Most of these proteins are sequence-specific DNA-binding transcription factors. The homeobox domain is also very similar to a region of the yeast mating type proteins. These are sequence-specific DNA-binding proteins that act as master switches in yeast differentiation by controlling gene expression in a cell type-specific fashion.

A schematic representation of the homeobox domain is shown below. The helix-turn-helix region is shown by the symbols 'H' (for helix), and 't' (for turn).

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The pattern detects homeobox sequences 24 residues long and spans positions 34 to 57 of the homeobox domain. The consensus pattern is as follows: [LIVMFYG]-[ASLVR]-x(2)-[LIVMSTACN]-x-[LIVM]-x(4)-[LIV]-[RKNQESTAIY]-[LIVFSTNKH]-W-[FYVC]-x-[NDQTAH]-x(5)-[RKNAIMW].

MAP kinase kinase (MAPKK). MAP kinases (MAPK) are involved in signal transduction, and are important in cell cycle and cell growth controls. The MAP kinase kinases (MAPKK) are dual-specificity protein kinases which phosphorylate and activate MAP kinases. MAPKK homologues have been found in yeast, invertebrates, amphibians, and mammals. Moreover, the MAPKK/MAPK phosphorylation switch constitutes a basic module activated in distinct pathways in yeast and in vertebrates. MAPKK regulation studies have led to the discovery of at least four MAPKK convergent pathways in higher organisms. One of these is similar to the yeast pheromone response pathway which includes the stell protein kinase. Two other pathways require the activation of either one or both of the serine/threonine kinase-encoded oncogenes c-Raf-1 and c-Mos. Additionally, several studies suggest a possible effect of the cell cycle control regulator cyclin-dependent kinase 1 (cdc2) on MAPKK activity. Finally, MAPKKs are apparently essential transducers through which signals must pass before reaching the nucleus. For review, see, e.g., Biologique Biol Cell (1993) 79:193-207; Nishida et al., Trends Biochem Sci (1993) 18:128-31; Ruderman Curr Opin Cell Biol (1993) 5:207-13; Dhanasekaran et al., Oncogene (1998) 17:1447-55; Kiefer et al., Biochem Soc Trans (1997) 25:491-8; and Hill, Cell Signal (1996) 8:533-44.

Those skilled in the art will recognize, or be able to ascertain, using not more than routine experimentation, many equivalents to the specific embodiments of the invention described herein. Such specific embodiments and equivalents are intended to be encompassed by the following claims.

All publications and patent applications cited in this specification are herein incorporated by reference as if each individual publication or patent application were specifically and individually indicated to be incorporated by reference. The citation of any publication is for its disclosure prior to the filing date and should not be construed as an admission that the present invention is not entitled to antedate such publication by virtue of prior invention.

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Although the foregoing invention has been described in some detail by way of illustration and example for purposes of clarity of understanding, it is readily apparent to those of ordinary skill in the art in light of the teachings of this invention that certain changes and modifications may be made thereto without departing from the spirit or scope of the appended claims.

Deposit Information:

The following materials were deposited with the American Type Culture Collection: CMCC = (Chiron Master Culture Collection)

Cell Lines Deposited with ATCC

Cell Line	Deposit Date	ATCC Accession No.	CMCC Accession No.
KM12L4-A	March 19, 1998	CRL-12496	11606
Km12C	May 15, 1998	CRL-12533	11611
MDA-MB-231	May 15, 1998	CRL-12532	10583
MCF-7	October 9, 1998	CRL-12584	10377

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cDNA Library ES1 - ATCC# Deposit Date - December 22, 1998

Clone Name	Cluster ID	Sequence Name
M00001395A:C03	4016	79.A1.sp6:130016.Seq
M00001395A:C03	4016	RTA00000118A.c.4.1
M00001449A:D12	3681	RTA00000131A.g.15.2
M00001449A:D12	3681	79.E1.sp6:130064.Seq
M00001452A:D08	1120	79.C2.sp6:130041.Seq
M00001452A:D08	1120	RTA00000118A.p.15.3
M00001513A:B06	4568	79.D4.sp6:130055.Seq
M00001513A:B06	4568	RTA00000122A.d.15.3
M00001517A:B07	4313	79.F4.sp6:130079.Seq
M00001517A:B07	4313	RTA00000122A.n.3.1
M00001533A:C11	2428	RTA00000123A.1.21.1
M00001533A:C11	2428	79.A5.sp6:130020.Seq
M00001533A:C11	2428	RTA00000123A.1.21.1.Seq_THC205063
M00001542A:A09	22113	79.F5.sp6:130080.Seq
M00001542A:A09	22113	RTA00000125A.c.7.1

Cl M	,	
Clone Name	Cluster ID	Sequence Name
M00001343C:F10	2790	80.E1.sp6:130256.Seq
M00001343C:F10	2790	RTA00000177AF.e.2.1.Seq_THC229461
M00001343C:F10	2790	RTA00000177AF.e.2.1
M00001343D:H07	23255	100.C1.sp6:131446.Seq
M00001343D:H07	23255	RTA00000177AF.e.14.3.Seq_THC228776
M00001343D:H07	23255	80.F1.sp6:130268.Seq
M00001343D:H07	23255	RTA00000177AF.e.14.3
M00001345A:E01	6420	172.E1.sp6:133925.Seq
M00001345A:E01	6420	RTA00000177AF.f.10.3
M00001345A:E01	6420	RTA00000177AF.f.10.3.Seq_THC226443
M00001345A:E01	6420	80.G1.sp6:130280.Seq
M00001347A:B10	13576	80.D2.sp6:130245.Seq
M00001347A:B10	13576	100.E1.sp6:131470.Seq
M00001347A:B10	13576	RTA00000177AF.g.16.1
M00001353A:G12	8078	80.E3.sp6:130258.Seq
M00001353A:G12	8078	RTA00000177AR.I.13.1
M00001353A:G12	8078	172.C3.sp6:133903.Seq
M00001353D:D10	14929	RTA00000177AF.m.1.2
M00001353D:D10	14929	80.F3.sp6:130270.Seq
M00001353D:D10	14929	172.D3.sp6:133915.Seq
M00001361A:A05	4141	80.B4.sp6:130223.Seq
M00001361A:A05	4141	RTA00000177AF.p.20.3
M00001362B:D10	5622	80.D4.sp6:130247.Seq
M00001362B;D10	5622	RTA00000178AF.a.11.1

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cDNA Library ES3 - ATCC# Deposit Date - December 22, 1998

	,	
Clone Name	Cluster ID	Sequence Name
M00001362C:H11	945	RTA00000178AR.a.20.1
M00001362C:H11	945	100.E4.sp6:131473.Seq
M00001362C:H11	945	80.E4.sp6:130259.Seq
M00001362C:H11	945	180.C2.sp6:135940.Seq
M00001376B:G06	17732	RTA00000178AR.i.2.2
M00001376B:G06	17732	80.B5.sp6:130224.Seq
M00001387A:C05	2464	80.D6.sp6:130249.Seq
M00001387A:C05	2464	RTA00000178AF.n.18.1
M00001412B:B10	8 551	RTA00000179AF.p.21.1
M00001412B:B10	8551	80.G7.sp6:130286.Seq
M00001415A:H06	13538	80.B8.sp6:130227.Seq
M00001415A:H06	13538	RTA00000180AF.a.24.1
M00001416B:H11	8847	80.C8.sp6:130239.Seq
M00001416B:H11	8847	RTA00000180AF.b.16.1
M00001429D:D07	40392	RTA00000180AF.j.8.1
M00001429D:D07	40392	80.H9.sp6:130300.Seq
M00001448D:H01	36313	80.A11.sp6:130218.Seq
M00001448D:H01	36313	RTA00000181AF.e.23.1

Clone Name	Cluster ID	Sequence Name
M00001463C:B11	19	RTA00000182AF.b.7.1
M00001463C:B11	19	89.D1.sp6:130703.Seq
M00001470A:B10	1037	89.F2.sp6:130728.Seq
M00001470A:B10	1037	RTA00000121A.f.8.1
M00001497A:G02	2623	89.F3.sp6:130729.Seq
M00001497A:G02	2623	RTA00000183AF.a.6.1
M00001500A:E11	2623	RTA00000183AF.b.14.1
M00001500A:E11	2623	89.A4.sp6:130670.Seq
M00001501D:C02	9685	RTA00000183AF.c.11.1.Seq THC109544
M00001501D:C02	9685	RTA00000183AF.c.11.1
M00001501D:C02	9685	89.C4.sp6:130694.Seq
M00001504C:H06	6974	89.F4.sp6:130730.Seq
M00001504C:H06	6974	RTA00000183AF.d.9.1
M00001504C:H06	6974	RTA00000183AF.d.9.1.Seq THC223129
M00001504D:G06	6420	173.F5.SP6:134133.Seq
M00001504D:G06	6420	89.G4.sp6:130742.Seq
M00001504D:G06	6420	RTA00000183AF.d.11.1.Seq_THC226443
M00001504D:G06	6420	RTA00000183AF.d.11.1
M00001528A:C04	35555	89.B6.sp6:130684.Seq
M00001528A:C04	7337	RTA00000123A.b.17.1
M00001528A:C04	35555	184.A5.sp6:135530.Seq
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Clone Name	Cluster ID	Sequence Name
M00001537B:G07	3389	RTA00000183AF.m.19.1
M00001537B:G07	3389	89.A8.sp6:130674.Seq
M00001541A:D02	3765	89.C8.sp6:130698.Seq
M00001541A:D02	3765	RTA00000135A.d.1.1
M00001544B:B07	6974	89.A9.sp6:130675.Seq
M00001544B:B07	6974	RTA00000184AF.a.15.1
M00001546A:G11	1267	89.D9.sp6:130711.Seq
M00001546A:G11	1267	RTA00000125A.o.5.1
M00001549B:F06	4193	89.G9.sp6:130747.Seq
M00001549B:F06	4193	RTA00000184AF.e.13.1
M00001556A:F11	1577	173.C9.SP6:134101.Seq
M00001556A:F11	1577	89.F11.sp6:130737.Seq
M00001556A:F11	1577	RTA00000184AF.i.23.1
M00001556B:C08	4386	RTA00000184AF.j.4.1
M00001556B:C08	4386	89.H11.sp6:130761.Seq

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Clone Name	Cluster ID	Sequence Name
M00001563B:F06	102	RTA00000184AF.o.5.1
M00001563B:F06	102	90.B1.sp6:130871.Seq
M00001571C:H06	5749	90.E1.sp6:130907.Seq
M00001571C:H06	5749	RTA00000185AF.a.19.1
M00001594B:H04	260	90.D2.sp6:130896.Seq
M00001594B:H04	260	RTA00000185AR.i.12.2
M00001597C:H02	4837	90.E2.sp6:130908.Seq
M00001597C:H02	4837	RTA00000185AR.k.3.2
M00001624C:F01	4309	90.C4.sp6:130886.Seq
M00001624C:F01	4309	RTA00000186AF.e.22.1
M00001679A:A06	6660	90.F6.sp6:130924.Seq
M00001679A:A06	6660	122.B5.sp6:132089.Seq
M00001679A:A06	6660	RTA00000187AF.h.15.1
M00003759B:B09	697	90.G8.sp6:130938.Seq
M00003759B:B09	697	RTA00000188AF.d.6.1
M00003759B:B09	697	RTA00000188AF.d.6.1.Seq THC178884
M00003844C:B11	6539	176.D9.sp6:134556.Seq
M00003844C:B11	6539	RTA00000189AF.d.22.1
M00003844C:B11	6539	90.B10.sp6:130880.Seq
M00003857A:G10	3389	90.A11.sp6:130869.Seq
M00003857A:G10	3389	RTA00000189AF.g.3.1
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Clone Name	Cluster ID	Sequence Name
M00003914C:F05	3900	99.E1.sp6:131278.Seq
M00003914C:F05	3900	RTA00000190AF.g.13.1
M00003922A:E06	23255	RTA00000190AF.j.4.1
M00003922A:E06	23255	99.F1.sp6:131290.Seq
M00003922A:E06	23255	RTA00000190AF.j.4.1.Seq_THC228776
M00003983A:A05	9105	99.C3.sp6:131256.Seq
M00003983A:A05	9105	RTA00000191AF.a.21.2
M00004028D:A06	6124	RTA00000191AR.e.2.3
M00004028D:A06	6124	99.D3.sp6:131268.Seq
M00004031A:A12	9061	RTA00000191AR.e.11.2
M00004031A:A12	9061	RTA00000191AR.e.11.3
M00004087D:A01	6880	RTA00000191AF.m.20.1
M00004087D:A01	6880	99.A5.sp6:131234.Seq
M00004108A:E06	4937	99.E5.sp6:131282.Seq
M00004108A:E06	4937	RTA00000191AF.p.21.1
M00004114C:F11	13183	123.D5.sp6:132305.Seq
M00004114C:F11	13183	RTA00000192AF.a.24.1
M00004114C:F11	13183	99.G5.sp6:131306.Seq
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cDNA Library ES8 - ATCC#

Deposit Date - December 22, 1998

Clone Name	Cluster ID	Sequence Name
M00004146C:C11	5257	99.B6.sp6:131247.Seq
M00004146C:C11	5257	177.F5.sp6:134768.Seq
M00004146C:C11	5257	RTA00000192AF.f.3.1
M00004146C:C11	5257	RTA00000192AF.f.3.1.Seq_THC213833
M00004157C:A09	6455	RTA00000192AF.g.23.1
M00004157C:A09	6455	99.D6.sp6:131271.Seq
M00004157C:A09	6455	123.E7.sp6:132319.Seq
M00004172C:D08	11494	RTA00000192AF.j.6.1
M00004172C:D08	11494	99.G6.sp6:131307.Seq
M00004172C:D08	11494	177.E6.sp6:134757.Seq
M00004229B:F08	6455	RTA00000193AF.b.9.1
M00004229B:F08	6455	99.C8.sp6:131261.Seq

cDNA Library ES9 - ATCC#

Deposit Date - December 22, 1998

Clone Name	Cluster ID	Sequence Name
M00001466A:E07	4275	RTA00000120A.j.14.1
M00001531A:H11		89.F6.sp6:130732.Seq
M00001531A:H11		RTA00000123A.g.19.1
M00001551A:B10	6268	79.G9.sp6:130096.Seq
M00001551A:B10	6268	184.C12.sp6:135561.Seq
M00001551A:B10	6268	RTA00000126A.o.23.1
M00001552A:B12	307	RTA00000136A.o.4.2
M00001552A:B12	307	79.C7.sp6:130046.Seq
M00001556A:H01	15855	RTA00000184AF.j.1.1
M00001586C:C05	4623	RTA00000185AF.f.4.1
M00001604A:B10	1399	79.G8.sp6:130095.Seq
M00001604A:B10	1399	RTA00000129A.o.10.1
M00003879B:C11	5345	RTA00000189AF.I.19.1
M00003879B:C11	5345	90.B12.sp6:130882.Seq
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Clone Name	Cluster ID	Sequence Name	***
M00001358C:C06		RTA00000177AF.o.4.3	
M00001388D:G05	5832	80.F6.sp6:130273.Seq	
M00001388D:G05	5832	RTA00000178AF.o.23.1	
M00001394A:F01	6583	RTA00000179AF.d.13.1	
M00001394A:F01	6583	172.B8.sp6:133896.Seq	
M00001394A:F01	6583	80.H6.sp6:130297.Seq	
M00001429A:H04	2797	RTA00000180AF.i.19.1	
M00001447A:G03	10717	RTA00000181AF.d.10.1	
M00001448D:C09	8	80.H10.sp6:130301.Seq	
M00001448D:C09	8	RTA00000181AF.e.17.1	
M00001448D:C09	8	100.B11.sp6:131444.Seq	
M00001454D:G03	68 9	RTA00000181AR.I.22.1	

cDNA Library ES11 - ATCC#

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Clone Name	Cluster ID	Sequence Name
M00003975A:G11	12439	RTA00000190AF.o.24.1
M00003978B:G05	5693	RTA00000190AF.p.17.2.Seq_THC173318
M00003978B:G05	5693	RTA00000190AF.p.17.2
M00004059A:D06	5417	RTA00000191AF.h.19.1
M00004068B:A01	3706	99.C4.sp6:131257.Seq
M00004068B:A01	3706	RTA00000191AF.i.17.2
M00004205D:F06		99.E7.sp6:131284.Seq
M00004205D:F06		177.G7.sp6:134782.Seq
M00004205D:F06		RTA00000192AF.o.11.1
M00004212B:C07	2379	RTA00000192AF.p.8.1
M00004223A:G10	16918	RTA00000193AF.a.16.1

cDNA Library ES12 - ATCC#

Deposit Date - December 22, 1998

Clone Name	Cluster ID	Sequence Name	
M00004223B:D09	7899	RTA00000193AF.a.17.1	
M00004249D:G12		RTA00000193AF.c.22.1	
M00004251C:G07		RTA00000193AF.d.2.1	
M00004372 A · A 03	2030	RTA00000193AF m 20 1	

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Clone Name	Cluster ID	Sequence Name
M00001340B:A06	17062	80.A1.sp6:130208.Seq
M00001340B:A06	17062	RTA00000177AF.b.8.4
M00001340D:F10	11589	80.B1.sp6:130220.Seq
M00001340D:F10	11589	RTA00000177AF.b.17.4
M00001341A:E12	4443	80.C1.sp6:130232.Seq
M00001341A:E12	4443	RTA00000177AF.b.20.4
M00001342B:E06	39805	80.D1.sp6:130244.Seq
M00001342B:E06	39805	RTA00000177AF.c.21.3
M00001346A:F09	5007	RTA00000177AF.g.2.1
M00001346A:F09	5007	80.H1.sp6:130292.Seq
M00001346D:G06	5779	RTA00000177AF.g.14.3
M00001346D:G06	5779	RTA00000177AF.g.14.1
M00001348B:B04	16927	80.E2.sp6:130257.Seq
M00001348B:B04	16927	RTA00000177AF.h.9.3
M00001348B:G06	16985	RTA00000177AF.h.10.1
M00001348B:G06	16985	80.F2.sp6:130269.Seq
M00001349B:B08	3584	RTA00000177AF.h.20.1
M00001349B:B08	3584	80.G2.sp6:130281.Seq
M00001350A:H01	7187	100.C2.sp6:131447.Seq
M00001350A:H01	7187	80.A3.sp6:130210.Seq
M00001350A:H01	7187	RTA00000177AF.i.8.2
M00001352A:E02	16245	RTA00000177AF.k.9.3
M00001352A:E02	16245	172.D2.sp6:133914.Seq
M00001352A:E02	16245	80.D3.sp6:130246.Seq
M00001355B:G10	14391	RTA00000177AF.m.17.3
M00001355B:G10	14391	80.G3.sp6:130282.Seq
M00001355B:G10	14391	172.H3.sp6:133963.Seq
M00001355B:G10	14391	100.E3.sp6:131472.Seq
M00001361D:F08	2379	80.C4.sp6:130235.Seq
M00001361D:F08	2379	RTA00000178AF.a.6.1
M00001365C:C10	40132	RTA00000178AF.c.7.1
M00001365C:C10	40132	80.F4.sp6:130271.Seq
M00001368D:E03		80.G4.sp6:130283.Seq
M00001368D:E03		RTA00000178AF.d.20.1
M00001370A:C09	6867	80.H4.sp6:130295.Seq
M00001370A:C09	6867	RTA00000178AF.e.12.1
M00001371C:E09	7172	100.A5.sp6:131426.Seq
M00001371C:E09	7172	RTA00000178AF.f.9.1
M00001371C:E09	7172	80.A5.sp6:130212.Seq
M00001378B:B02	39833	80.C5.sp6:130236.Seq
M00001378B:B02	39833	RTA00000178AF.i.23.1
M00001379A:A05	1334	80.D5.sp6:130248.Seq
M00001379A:A05	1334	RTA00000178AF.j.7.1
M00001380D:B09	39886	RTA00000178AF.j.24.1
M00001380D:B09	39886	80.E5.sp6:130260.Seq
M00001381D:E06	0,000	80.F5.sp6:130272.Seq
M00001381D:E06		RTA00000178AF.k.16.1
M00001381D:200	22979	80.G5.sp6:130284.Seq
M00001302C:A02	22979	RTA00000178AF.k.22.1
M00001384B:A11		80.B6.sp6:130225.Seq
M00001304B:A11		RTA00000178AF.m.13.1
M00001304B:A11	5178	80.C6.sp6:130237.Seq
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M00001386C:B12	5178	RTA00000178AF.n.10.1
M00001387B:G03	7587	80.E6.sp6:130261.Seq
M00001387B:G03	7587	RTA00000178AF.n.24.1
M00001389A:C08	16269	RTA00000178AF.p.1.1
M00001389A:C08	16269	80.G6.sp6:130285.Seq
M00001396A:C03	4009	172.D8.sp6:133920.Seq
M00001396A:C03	4009	80.A7.sp6:130214.Seq
M00001396A:C03	4009	RTA00000179AF.e.20.1
M00001400B:H06		172.B9.sp6:133897.Seq
M00001400B:H06		80.B7.sp6:130226.Seq
M00001400B:H06		RTA00000179AF.j.13.1
M00001400B:H06		RTA00000179AF.j.13.1.Seq_THC105720
M00001402A:E08	39563	80.C7.sp6:130238.Seq
M00001402A:E08	39563	RTA00000179AF.k.20.1
M00001407B:D11	5556	RTA00000179AF.n.10.1
M00001407B:D11	5556	80.D7.sp6:130250.Seq
M00001410A:D07	7005	180.H5.sp6:136003.Seq
M00001410A:D07	7005	RTA00000179AF.o.22.1
M00001410A:D07	7005	80.F7.sp6:130274.Seq
M00001414A:B01		RTA00000180AF.a.9.1
M00001414A:B01		80.H7.sp6:130298.Seq
M00001414C:A07		80.A8.sp6:130215.Seq
M00001414C:A07		RTA00000180AF.a.11.1
M00001416A:H01	7674	79.C1.sp6:130040.Seq
M00001416A:H01	7674	RTA00000118A.g.9.1
M00001417A:E02	36393	RTA00000180AF.c.2.1
M00001417A:E02	36393	80.D8.sp6:130251.Seq
M00001423B:E07	15066	RTA00000180AF.e.24.1
M00001423B:E07	15066	80.H8.sp6:130299.Seq
M00001424B:G09	10470	80.A9.sp6:130216.Seq
M00001424B:G09	10470	RTA00000180AF.f.18.1
M00001425B:H08	22195	RTA00000180AF.g.7.1
M00001425B:H08	22195	80.B9.sp6:130228.Seq
M00001426B:D12		RTA00000180AF.g.22.1
M00001426B:D12		80.C9.sp6:130240.Seq
M00001426D:C08	4261	80.D9.sp6:130252.Seq
M00001426D:C08	4261	RTA00000180AF.h.5.1
M00001428A:H10	84182	100.G9.sp6:131502.Seq
M00001428A:H10	84182	RTA00000180AF.h.19.1
M00001428A:H10	84182	80.E9.sp6:130264.Seq
M00001449A:A12	5857	80.B11.sp6:130230.Seq
M00001449A:A12	5857	RTA00000118A.g.14.1
M00001449A:B12	41633	80.C11.sp6:130242.Seq
M00001449A:B12	41633	RTA00000118A.g.16.1
M00001449A:G10	36535	RTA00000181AF.f.5.1
M00001449A:G10	36535	80.D11.sp6:130254.Seq
M00001449A:G10	36535	100.D11.sp6:131468.Seq
M00001449C:D06	86110	RTA00000181AF.f.12.1
M00001449C:D06	86110	80.E11.sp6:130266.Seq
M00001450A:A02	39304	RTA00000118A.j.21.1.Seq_THC151859
M00001450A:A02	39304	RTA00000118A.j.21.1
M00001450A:A02	39304	79.F1.sp6:130076.Seq
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Clone Name	Cluster ID	Sequence Name
M00001450A:A02	39304	180.G9.sp6:135995.Seq
M00001450A:A11	32663	80.F11.sp6:130278.Seq
M00001450A:A11	32663	RTA00000118A.I.8.1
M00001450A:B12	82498	100.F11.sp6:131492.Seq
M00001450A:B12	82498	RTA00000118A.m.10.1
M00001450A:B12	82498	79.G1.sp6:130088.Seq
M00001450A:D08	27250	80.G11.sp6:130290.Seq
M00001450A:D08	27250	180.B10.sp6:135936.Seq
M00001450A:D08	27250	RTA00000181AF.g.10.1
M00001452A:B04	84328	RTA00000118A.p.10.1
M00001452A:B04	84328	79.A2.sp6:130017.Seq
M00001452A:B12	86859	RTA00000118A.p.8.1
M00001452A:B12	86859	79.B2.sp6:130029.Seq
M00001452A:F05	85064	RTA00000131A.m.23.1
M00001452A:F05	85064	79.D2.sp6:130053.Seq
M00001452C:B06	16970	80.H11.sp6:130302.Seq
M00001452C:B06	16970	100.C12.sp6:131457.Seq
M00001452C:B06	16970	RTA00000181AR.i.18.2
M00001453A:E11	16130	80.A12.sp6:130219.Seq
M00001453A:E11	16130	100.D12.sp6:131469.Seq
M00001453A:E11	16130	RTA00000119A.c.13.1
M00001453C:F06	16653	80.B12.sp6:130231.Seq
M00001453C:F06	16653	RTA00000181AF.k.5.3
M00001454A:A09	83103	RTA00000119A.e.24.2
M00001454A:A09	83103	79.G2.sp6:130089.Seq
M00001454B:C12	7005	121.D1.sp6:131917.Seq
M00001454B:C12	7005	RTA00000181AF.k.24.1
M00001454B:C12	7005	80.C12.sp6:130243.Seq
M00001455B:E12	13072	80.F12.sp6:130279.Seq
M00001455B:E12	13072	RTA00000181AR.m.5.2
M00001460A:F06	2448	89.A1.sp6:130667.Seq
M00001460A:F06	2448	RTA00000119A.j.21.1
M00001461A:D06	1531	89.C1.sp6:130691.Seq
M00001461A:D06	1531	RTA00000119A.o.3.1
M00001465A:B11	10145	79.F3.sp6:130078.Seq
M00001465A:B11	10145	RTA00000120A.g.12.1
M00001467A:B07	38759	89.F1.sp6:130727.Seq
M00001467A:B07	38759	RTA00000120A.m.12.3
M00001467A:D04	39508	RTA0000120A.o.2.1
M00001467A:D04	39508	89.G1.sp6:130739.Seq
M00001467A:E10	39442	89.A2.sp6:130668.Seq
M00001467A:E10	39442	RTA00000120A.o.21.1
M00001467A:E10	7589	RTA00000120A.p.23.1
M00001468A:F05	7589	89.B2.sp6:130680.Seq
M00001468A:103	7309	RTA0000121A.c.10.1
M00001469A:A01		
M00001469A:A01 M00001469A:C10	12001	89.C2.sp6:130692.Seq
	12081	89.D2.sp6:130704.Seq
M00001469A:C10	12081	RTA00000133A.d.14.2
M00001469A:H12	19105	89.E2.sp6:130716.Seq
M00001469A:H12	19105	RTA00000133A.e.15.1
M00001470A:C04	39425 39425	89.G2.sp6:130740.Seq
M00001470A:C04	39425	RTA00000133A.f.1.1
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Clone Name	Cluster ID	Sequence Name
M00001471A:B01	39478	89.H2.sp6:130752.Seq
M00001471A:B01	39478	RTA00000133A.i.5.1
M00001487B:H06		RTA00000182AF.1.15.1
M00001487B:H06		89.B3.sp6:130681.Seq
M00001488B:F12		RTA00000182AF.1.20.1
M00001488B:F12		89.C3.sp6:130693.Seq
M00001494D:F06	7206	RTA00000182AF.o.15.1
M00001494D:F06	7206	89.E3.sp6:130717.Seq
M00001499B:A11	10539	RTA00000183AF.a.24.1
M00001499B:A11	10539	89.G3.sp6:130741.Seq
M00001499B:A11	10539	173.B5.SP6:134085.Seq
M00001500A:C05	5336	RTA00000183AF.b.13.1
M00001500A:C05	5336	89.H3.sp6:130753.Seq
M00001504A:E01		RTA00000183AF.c.24.1
M00001504A:E01		89.D4.sp6:130706.Seq
M00001504A:E01		RTA00000183AF.c.24.1.Seq_THC125912
M00001504C:A07	10185	RTA00000183AF.d.5.1
M00001504C:A07	10185	89.E4.sp6:130718.Seq
M00001505C:C05		89.H4.sp6:130754.Seq
M00001505C:C05		RTA00000183AF.e.1.1
M00001506D:A09		89.A5.sp6:130671.Seq
M00001506D:A09		RTA00000183AF.e.23.1
M00001506D:A09		121.G6.sp6:131958.Seq
M00001507A:H05	39168	RTA00000121A.1.10.1
M00001507A:H05	39168	89.B5.sp6:130683.Seq
M00001535A:F10	39423	79.C5.sp6:130044.Seq
M00001535A:F10	39423	RTA00000134A.k.22.1
M00001541A:H03	39174	79.E5.sp6:130068.Seq
M00001541A:H03	39174	RTA00000124A.n.13.1
M00001544A:G02	19829	79.H5.sp6:130104.Seq
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M00001545A:D08	13864	79.B6.sp6:130033.Seq
M00001551A:F05	39180	RTA00000126A.n.8.2
M00001551A:F05	39180	79.A7.sp6:130022.Seq
M00001552A:D11	39458	RTA00000126A.p.15.2
M00001552A:D11	39458	79.D7.sp6:130058.Seq
M00001557A:F03	39490	RTA00000128A.b.4.1

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Clone Name	Cluster ID	Sequence Name
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M00001511A:H06	39412	89.C5.sp6:130695.Seq
M00001512A:A09	39186	89.D5.sp6:130707.Seq
M00001512A:A09	39186	RTA00000121A.p.15.1
M00001512D:G09	3956	89.E5.sp6:130719.Seq
M00001512D:G09	3956	173.H5.SP6:134157.Seq
M00001512D:G09	3956	RTA00000183AF.g.3.1
M00001513B:G03		RTA00000183AF.g.9.1
M00001513B:G03		89.F5.sp6:130731.Seq
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M00001513C:E08	14364	89.G5.sp6:130743.Seq
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M00001514C:D11	40044	RTA00000183AF.g.22.1.Seq_THC232899
M00001514C:D11	40044	89.H5.sp6:130755.Seq
M00001518C:B11	8952	89.A6.sp6:130672.Seq
M00001518C:B11	8952	RTA00000183AF.h.15.1
M00001528B:H04	8358	89.D6.sp6:130708.Seq
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M00001531A:D01	38085	89.E6.sp6:130720.Seq
M00001534A:C04	16921	RTA00000183AF.k.6.1
M00001534A:C04	16921	89.H6.sp6:130756.Seq
M00001534A:D09	5097	RTA00000134A.k.1.1
M00001534A:D09	5097	RTA00000134A.k.1.1.Seq_THC215869
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M00001534C:A01	4119	89.C7.sp6:130697.Seq
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M00001537A:F12	39420	89.H7.sp6:130757.Seq
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M00001540A:D06	8286	89.B8.sp6:130686.Seq
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M00001542A:E06	39453	89.E8.sp6:130722.Seq
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M00001548A:E10	5892	89.E9.sp6:130723.Seq
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M00001549C:E06	16347	89.H9.sp6:130759.Seq
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M00001550A:A03	7239	89.A10.sp6:130676.Seq
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M00001550A:G01	5175	RTA00000184AF.f.3.1
M00001550A:G01	5175	89.B10.sp6:130688.Seq
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M00001551C:G09	3266	89.D10.sp6:130712.Seq
M00001553A:H06	8298	RTA00000127A.d.19.1
M00001553A:H06	8298	89.G10.sp6:130748.Seq
M00001553B:F12	4573	89.H10.sp6:130760.Seq
M00001553B:F12	4573	RTA00000184AF.h.9.1
M00001555A:B02	39539	RTA00000127A.i.21.1
M00001555A:B02	39539	89.B11.sp6:130689.Seq
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M00001598A:G03	16999	90.G2.sp6:130932.Seq
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M00001608D:A11		RTA00000185AF.n.12.1
M00001608D:A11		90.D3.sp6:130897.Seq
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M00001619C:F12	40314	90.G3.sp6:130933.Seq
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M00001621C:C08	40044	RTA00000186AF.d.1.1.Seq_THC232899
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M00001621C:C08	40044	122.E1.sp6:132121.Seq
M00001623D:F10	13913	RTA00000186AF.e.6.1
M00001623D:F10	13913	90.A4.sp6:130862.Seq
M00001632D:H07		RTA00000186AF.h.14.1.Seq_THC112525
M00001632D:H07		RTA00000186AF.h.14.1
M00001632D:H07		90.E4.sp6:130910.Seq
M00001632D:H07	40171	176.A3.sp6:134514.Seq
M00001644C:B07	39171	RTA00000186AF.1.7.1
M00001644C:B07	39171	90.F4.sp6:130922.Seq
M00001644C:B07	39171	217.A12.sp6:139369.Seq
M00001645A:C12	19267	RTA00000186AF.1.12.1.Seq_THC178183
M00001645A:C12	19267	176.G3.sp6:134586.Seq
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M00001645A:C12	19267	90.G4.sp6:130934.Seq
M00001648C:A01	4665	90.H4.sp6:130946.Seq
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M00001657D:F08	76760 76760	90.C5.sp6:130887.Seq
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M00001662C:A09	23218	RTA00000187AR.c.5.2 90.D5.sp6:130899.Seq
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M00001663A:E04	35702 35702	RTA00000187AR.c.15.2
M00001669B:F02	6468	90.F5.sp6:130923.Seq
M00001009B:F02	6468	RTA00000187AF.d.15.1
M00001609B:102 M00001670C:H02	14367	90.G5.sp6:130935.Seq
M00001070C:1102 M00001670C:H02	14367	RTA00000187AF.e.8.1
M00001070C:1102 M00001673C:H02	7015	90.H5.sp6:130947.Seq
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M00001675A:C09	8773	90.A6.sp6:130864.Seq
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M00001676B:F05	11460	RTA00000187AF.g.12.1
M00001676B:F05	11460	90.B6.sp6:130876.Seq
M00001676B:F05	11460	219.F2.sp6:139035.Seq
M00001677D:A07	7570	90.D6.sp6:130900.Seq
M00001677D:A07	7570	RTA00000187AF.g.24.1
M00001677D:A07	7570	RTA00000187AF.g.24.1.Seq_THC168636
M00001678D:F12	4416	90.E6.sp6:130912.Seq
M00001678D:F12	4416	RTA00000187AF.h.13.1
M00001679A:F10	26875	RTA00000187AF.i.1.1
M00001679A:F10	26875	90.A7.sp6:130865.Seq
M00001679B:F01	6298	90.B7.sp6:130877.Seq
M00001679B:F01	6298	RTA00000187AR.i.10.2
M00001680D:F08	10539	90.F7.sp6:130925.Seq
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M00001680D:F08	10539	RTA00000187AF.l.7.1
M00001682C:B12		90.G7.sp6:130937.Seq
M00001682C:B12	17055	RTA00000187AF.m.3.1
M00001682C:B12	17055	176.D6.sp6:134553.Seq
M00001688C:F09	5382	90.A8.sp6:130866.Seq
M00001688C:F09	5382	RTA00000187AF.m.23.2
M00001693C:G01	4393	RTA00000187AF.n.17.1
M00001693C:G01	4393	90.B8.sp6:130878.Seq
M00001716D:H05		RTA00000187AF.o.6.1
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M00003741D:C09		RTA00000187AF.o.24.1
M00003747D:C05		RTA00000187AF.p.19.1
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M00003747D:C05		RTA00000187AF.p.19.1.Seq_THC108482
M00003747D:C05	11476	219.H8.sp6:139065.Seq
M00003754C:E09		90.F8.sp6:130926.Seq
M00003754C:E09		RTA00000188AF.b.12.1
M00003761D:A09		RTA00000188AF.d.11.1
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M00003761D:A09		RTA00000188AF.d.11.1.Seq_THC212094
M00003762C:B08	17076	RTA00000188AF.d.21.1.Seq_THC208760
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M00003774C:A03	67907	90.C9.sp6:130891.Seq
M00003784D:D12		RTA00000188AF.i.8.1
M00003784D:D12		90.D9.sp6:130903.Seq
M00003839A:D08		RTA00000189AF.c.18.1
M00003839A:D08		90.A10.sp6:130868.Seq
M00003851B:D08		90.D10.sp6:130904.Seq
M00003851B:D08		RTA00000189AF.f.7.1
M00003851B:D10	13595	90.E10.sp6:130916.Seq
M00003851B:D10		RTA00000189AF.f.8.1
M00003853A:D04	5619	90.F10.sp6:130928.Seq
M00003853A:D04	5619	RTA00000189AF.f.17.1
M00003853A:F12	10515	90.G10.sp6:130940.Seq
M00003853A:F12	10515	RTA00000189AF.f.18.1
M00003856B:C02	4622	90.H10.sp6:130952.Seq
M00003856B:C02	4622	RTA00000189AF.g.1.1
M00003857A:H03	4718	90.B11.sp6:130881.Seq
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M00003875C:G07	8479	90.G11.sp6:130941.Seq
M00003875C:G07	8479	RTA00000189AF.j.22.1
M00003875D:D11		90.H11.sp6:130953.Seq
M00003875D:D11		RTA00000189AF.j.23.1
M00003876D:E12	7798	90.A12.sp6:130870.Seq
M00003876D:E12	7798	RTA00000189AF.k.12.1
M00003906C:E10	9285	90.H12.sp6:130954.Seq
M00003906C:E10	9285	RTA00000190AF.d.7.1
M00003907D:A09	39809	99.A1.sp6:131230.Seq
M00003907D:A09	39809	RTA00000190AF.e.3.1.Seq_THC150217
M00003907D:A09	39809	RTA00000190AF.e.3.1
M00003907D:H04	16317	99.B1.sp6:131242.Seq
M00003907D:H04	16317	RTA00000190AF.e.6.1
M00003909D:C03	8672	RTA00000190AF.f.11.1
M00003909D:C03	8672	99.C1.sp6:131254.Seq
M00003968B:F06	24488	RTA00000190AF.n.16.1
M00003968B:F06	24488	99.C2.sp6:131255.Seq
M00003900B:100	40122	RTA00000190AF.n.23.1
M00003970C:B09	40122	RTA00000190AF.n.23.1.Seq_THC109227
M00003970C:B09	40122	99.D2.sp6:131267.Seq
M00003974D:E07	23210	RTA00000190AF.o.20.1
M00003974D:E07	23210	RTA00000190AF.o.20.1.Seq THC207240
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M00004035D:B06 M00004035D:B06	17036 17036	RTA00000191AF.f.13.1 99.A4.sp6:131233.Seq
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M00004081C:D10	15069	99.F4.sp6:131293.Seq
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M00004086D:G06	9285	99.H4.sp6:131317.Seq
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M00004105C:A04	7221	99.D5.sp6:131270.Seq
M00004105C:A04	7221	RTA00000191AF.p.9.1
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M00004185C:C03	11443	123.A8.sp6:132272.Seq
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M00004191D:B11		123.C8.sp6:132296.Seq
M00004197D:H01	8210	99.C7.sp6:131260.Seq
M00004197D:H01	8210	123.E8.sp6:132320.Seq
M00004197D:H01	8210	RTA00000192AF.n.13.1
M00004203B:C12	14311	99.D7.sp6:131272.Seq
M00004203B:C12	14311	RTA00000192AF.o.2.1
M00004214C:H05	11451	177.D8.sp6:134747.Seq
M00004214C:H05	11451	RTA00000192AF.p.17.1
M00004223D:E04	12971	RTA00000193AF.a.20.1
M00004223D:E04	12971	99.B8.sp6:131249.Seq
M00004269D:D06	4905	99.H8.sp6:131321.Seq
M00004269D:D06	4905	RTA00000193AF.e.14.1
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M00004295D:F12	16921	RTA00000193AF.h.15.1
M00004296C:H07	13046	99.E9.sp6:131286.Seq
M00004296C:H07	13046	RTA00000193AF.h.19.1
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M00004318C:D10	21847	99.H9.sp6:131322.Seq
M00004359B:G02		RTA00000193AF.m.5.1.Seq_THC173318
M00004359B:G02		RTA00000193AF.m.5.1
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Deposit Date - Decemi		
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M00001553D:D10	22814	89.A11.sp6:130677.Seq
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M00004138B:H02	13272	99.A6.sp6:131235.Seq
M00004138B:H02	13272	RTA00000192AF.e.3.1
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M00004169C:C12	5319	123.F7.sp6:132331.Seq
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M00004183C:D07	16392	RTA00000192AF.1.1.1.Seq_THC202071
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The above material has been deposited with the American Type Culture Collection, Rockville, Maryland, under the accession number indicated. This deposit will be maintained under the terms of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for purposes of Patent Procedure. The deposit will be maintained for a period of 30 years following issuance of this patent, or for the enforceable life of the patent, whichever is greater. Upon issuance of the patent, the deposit will be available to the public from the ATCC without restriction.

This deposit is provided merely as convenience to those of skill in the art, and is not an admission that a deposit is required under 35 U.S.C. §112. The sequence of the polynucleotides contained within the deposited material, as well as the amino acid sequence of the polypeptides encoded thereby, are incorporated herein by reference and are controlling in the event of any conflict with the written description of sequences herein. A license may

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be required to make, use, or sell the deposited material, and no such license is granted hereby.

Retrieval of Individual Clones from Deposit of Pooled Clones

Where the ATCC deposit is composed of a pool of cDNA clones, the deposit was prepared by first transfecting each of the clones into separate bacterial cells. The clones were then deposited as a pool of equal mixtures in the composite deposit. Particular clones can be obtained from the composite deposit using methods well known in the art. For example, a bacterial cell containing a particular clone can be identified by isolating single colonies, and identifying colonies containing the specific clone through standard colony hybridization techniques, using an oligonucleotide probe or probes designed to specifically hybridize to a sequence of the clone insert (e.g., a probe based upon unmasked sequence of the encoded polynucleotide having the indicated SEQ ID NO). The probe should be designed to have a T_m of approximately 80°C (assuming 2°C for each A or T and 4°C for each G or C). Positive colonies can then be picked, grown in culture, and the recombinant clone isolated. Alternatively, probes designed in this manner can be used to PCR to isolate a nucleic acid molecule from the pooled clones according to methods well known in the art, e.g., by purifying the cDNA from the deposited culture pool, and using the probes in PCR reactions to produce an amplified product having the corresponding desired polynucleotide sequence.

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4	3706	RTA00000191AF.i.17.2	M00004068B:A01
5	36535	RTA00000181AF.f.5.1	M00001449A:G10
6	3990	RTA00000183AF.j.11.1	M00001532B:A06
7	5319	RTA00000192AF.i.12.1	M00004169C:C12
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9	2623	RTA00000183AF.a.6.1	M00001497A:G02
10	7587	RTA00000178AF.n.24.1	M00001387B:G03
11	7065	RTA00000137A.g.6.1	M00001557A:D02
12	10539	RTA00000187AF.1.7.1	M00001680D:F08
13	27250	RTA00000181AF.g.10.1	M00001450A:D08
14	5556	RTA00000179AF.n.10.1	M00001407B:D11
15		RTA00000192AF.m.12.1	M00004191D:B11
16	8761	RTA00000184AF.k.12.1	M00001557D:D09
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24	16918	RTA00000193AF.a.16.1	M00004223A:G10
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29		RTA00000180AF.g.22.1	M00001426B:D12
30	13272	RTA00000192AF.e.3.1	M00004138B:H02
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33		RTA00000180AF.a.9.1	M00001414A:B01
34	5832	RTA00000178AF.o.23.1	M00001388D:G05
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36	76760	RTA00000187AF.a.15.1	M00001657D:F08
37	40132	RTA00000178AF.c.7.1	M00001365C:C10
38		RTA00000183AF.e.1.1	M00001505C:C05
39	4016	RTA00000118A.c.4.1	M00001395A:C03
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45	5325	RTA00000191AF.o.6.1	M00004093D:B12
46	5325	RTA00000191AF.o.6.2	M00004093D:B12
47	18957	RTA00000190AR.m.9.1	M00003958A:H02
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50	12170	RTA00000125A.h.18.4	M00001544A:E03
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52	19	RTA00000182AF.b.7.1	M00001463C:B11
53		RTA00000193AF.c.21.1	M00004249D:F10
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67	23001	RTA00000185AF.c.24.1	M00001578B:E04
68	6455	RTA00000192AF.g.23.1	M00004157C:A09
69	13595	RTA00000189AF.f.8.1	M00003851B:D10
70	39442	RTA00000120A.o.21.1	M00001467A:E10
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73	7005	RTA00000181AF.k.24.1	M00001454B:C12
74	6268	RTA00000126A.o.23.1	M00001551A:B10
75	16130	RTA00000119A.c.13.1	M00001453A:E11
76	23201	RTA00000187AF.a.14.1	M00001657D:C03
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79	2102	RTA00000193AF.n.7.1	M00004377C:F05
80	1058	RTA00000126A.e.20.3	M00001548A:H09
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87	5175	RTA00000184AF.f.3.1	M00001550A:G01
88	13576	RTA00000189AF.o.13.1	M00003885C:A02
89	7665	RTA00000134A.l.19.1	M00001535A:B01
90	16927	RTA00000177AF.h.9.3	M00001348B:B04
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92	2433	RTA00000191AF.a.15.2	M00003982C:C02
93	5097	RTA00000134A.k.1.1	M00001534A:D09
94	21847	RTA00000193AF.j.9.1	M00004318C:D10
95	3277	RTA00000138A.1.5.1	M00001624A:B06
96	5708	RTA00000184AF.g.12.1	M00001552B:D04
97	945	RTA00000178AR.a.20.1	M00001362C:H11
98	16269	RTA00000178AF.p.1.1	M00001389A:C08
99		RTA00000183AF.c.24.1	M00001504A:E01
100	16731	RTA00000181AF.a,20.1	M00001442C:D07
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124	39174	RTA00000124A.n.13.1	M00001541A:H03
125	24488	RTA00000124A.ii.13.1 RTA00000190AF.n.16.1	M00001941A.1103
126	8210	RTA00000192AF.n.13.1	M00003308B.100
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130	13183	RTA00000192AF.a.24.1	M00004114C:F11
131	5214	RTA00000186AF.g.11.1	M00001630B:H09
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133	3108	RTA00000188AF.d.24.1	M00003763A:F06
134	2464	RTA00000178AF.n.18.1	M00001387A:C05
135	36313	RTA00000181AF.e.23.1	M00001448D:H01
136	23255	RTA00000177AF.e.14.3	M00001343D:H07
137	7985	RTA00000182AR.j.2.1	M00001481D:A05
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139	22195	RTA00000180AF.g.7.1	M00001425B:H08
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141	26875	RTA00000187AF.i.1.1	M00001679A:F10
142	7187	RTA00000177AF.i.8.2	M00001350A:H01
143	86859	RTA00000118A.p.8.1	M00001452A:B12
144	4623	RTA00000185AF.f.4.1	M00001586C:C05
145		RTA00000121A.c.10.1	M00001469A:A01
146	10185	RTA00000183AF.d.5.1	M00001504C:A07
147		RTA00000183AF.p.4.1	M00001542B:B01
148	15069	RTA00000191AF.I.6.1	M00004081C:D10
149	39304	RTA00000118A.j.21.1	M00001450A:A02
150	8672	RTA00000190AF.f.11.1	M00003909D:C03
151	13576	RTA00000177AF.g.16.1	M00001347A:B10
152	6293	RTA00000185AF.e.11.1	M00001583D:A10
153	16977	RTA00000192AF.g.3.1	M00004151D:B08
154	5345	RTA00000189AF.I.19.1	M00003879B:C11
155	4905	RTA00000193AF.e.14.1	M00004269D:D06
156	17036	RTA00000191AF.j.10.1	M00004072B:B05
157	5417	RTA00000191AF.h.19.1	M00004059A:D06
158	7172	RTA00000178AF.f.9.1	M00001371C:E09
159	40044	RTA00000186AF.d.1.1	M00001621C:C08
160	4386	RTA00000184AF.j.4.1	M00001556B:C08
161	40044	RTA00000183AF.g.22.1	M00001514C:D11
162	9685	RTA00000183AF.c.11.1	M00001501D:C02
163	22155	RTA00000185AF.n.9.1	M00001608B:E03
164	10515	RTA00000189AF.f.18.1	M00003853A:F12
165	6539	RTA0000185AF.d.11.1	M00001579D:C03
166	15066	RTA0000180AF.e.24.1	M00001423B:E07
167	4261	RTA00000180AF.h.5.1	M00001426D:C08
168	13864	RTA0000125A.m.9.1	M00001420D:C08
169	6539	RTA000001257kiii.5.1	M0000134371:B00
107	0009		1.1000000 [O.D.]

WO 99/339	82		PCT/US98/27610
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170	11465	RTA00000185AF.m.19.1	M00001607A:E11
171	3266	RTA00000184AR.g.1.1	M00001551C:G09
172	102	RTA00000184AF.o.5.1	M00001563B:F06
173	16970	RTA00000181AR.i.18.2	M00001452C:B06
174	12971	RTA00000193AF.a.20.1	M00004223D:E04
175	5007	RTA00000177AF.g.2.1	M00001346A:F09
176	3765	RTA00000135A.d.1.1	M00001541A:D02
177	11294	RTA00000184AF.j.6.1	M00001556B:G02
1 78	3681	RTA00000131A.g.15.2	M00001449A:D12
1 79	9283	RTA00000181AR.m.21.2	M00001455D:F09
180	1 869 9	RTA00000182AF.m.16.1	M00001490B:C04
181	86110	RTA00000181AF.f.12.1	M00001449C:D06
182	39648	RTA00000178AR.1.8.2	M00001383A:C03
183	7337	RTA00000123A.b.17.1	M00001528A:C04
184	1334	RTA00000178AF.j.7.1	M00001379A:A05
185	17076	RTA00000188AF.d.21.1	M00003762C:B08
186	22794	RTA00000138A.b.5.1	M00001601A:D08
187	39171	RTA00000186AF.1.7.1	M00001644C:B07
188	8551	RTA00000179AF.p.21.1	M00001412B:B10
189	5857	RTA00000118A.g.14.1	M00001449A:A12
190	9443	RTA00000183AF.c.1.1	M00001500C:E04
191	9457	RTA00000193AF.i.14.2	M00004307C:A06
192	7206	RTA00000182AF.o.15.1	M00001494D:F06
193	22979	RTA00000178AF.k.22.1	M00001382C:A02
194	40455	RTA00000190AR.m.10.1	M00003958C:G10
195	7221	RTA00000191AF.p.9.1	M00004105C:A04
196		RTA00000191AF.j.9.1	M00004072A:C03
197	7239	RTA00000126A.m.4.2	M00001550A:A03
198	31587	RTA00000189AF.1.20.1	M00003879B:D10
199	16317	RTA00000190AF.e.6.1	M00003907D:H04
200	13576	RTA00000189AR.o.13.1	M00003885C:A02
201	5779	RTA00000177AF.g.14.3	M00001346D:G06
202	6124	RTA00000191AR.e.2.3	M00004028D:A06
203	9952	RTA00000180AF.c.20.1	M00001418B:F03
204		RTA00000188AF.i.8.1	M00003784D:D12
205	5779	RTA00000177AF.g.14.1	M00001346D:G06
206	39490	RTA00000128A.b.4.1	M00001557A:F03
207	4416	RTA00000187AF.h.13.1	M00001678D:F12
208	4009	RTA00000179AF.e.20.1	M00001396A:C03
209	5336	RTA00000183AF.b.13.1	M00001500A:C05
210	39186	RTA00000121A.p.15.1	M00001512A:A09
211	40122	RTA00000190AF.n.23.1	M00003970C:B09
212	12532	RTA00000190AF.g.2.1	M00003912B:D01

WO 99/339	982		PCT/US98/27610
SEQ ID NO:	Cluster ID	Sequence Name	Clone Name
213	8078	RTA00000177AR.I.13.1	M00001353A:G12
214	3900	RTA00000190AF.g.13.1	M00003914C:F05
215	7589	RTA00000120A.p.23.1	M00001468A:F05
216	8298	RTA00000127A.d.19.1	M00001553A:H06
217	4443	RTA00000177AF.b.20.4	M00001341A:E12
218	26295	RTA00000193AF.i.24.2	M00004312A:G03
219	3389	RTA00000183AF.m.19.1	M00001537B:G07
220	7015	RTA00000187AF.f.18.1	M00001673C:H02
221	8526	RTA00000180AF.d.1.1	M00001418D:B06
222	4665	RTA00000186AF.m.3.1	M00001648C:A01
223	1399	RTA00000129A.o.10.1	M00001604A:B10
224	9244	RTA00000127A.1.3.1	M00001556A:C09
225		RTA00000179AF.j.13.1	M00001400B:H06
226	82498	RTA00000118A.m.10.1	M00001450A:B12
227	35702	RTA00000187AR.c.15.2	M00001663A:E04
228	38759	RTA00000120A.m.12.3	M00001467A:B07
229	39648	RTA00000178AF.1.8.1	M00001383A:C03
230	19105	RTA00000133A.e.15.1	M00001469A:H12
231	85064	RTA00000131A.m.23.1	M00001452A:F05
232	9285	RTA00000191AF.m.18.1	M00004086D:G06
233	9285	RTA00000190AF.d.7.1	M00003906C:E10
234	39391	RTA00000138A.c.3.1	M00001604A:F05
235		RTA00000178AF.d.20.1	M00001368D:E03
236	39498	RTA00000119A.j.20.1	M00001460A:F12
237	7798	RTA00000189AF.k.12.1	M00003876D:E12
238	779 8	RTA00000189AF.c.18.1	M00003839A:D08
239	19829	RTA00000125A.h.24.4	M00001544A:G02
240		RTA00000188AF.d.11.1	M00003761D:A09
241	4275	RTA00000120A.j.14.1	M00001466A:E07
242	22113	RTA00000125A.c.7.1	M00001542A:A09
243	40314	RTA00000186AF.c.15.1	M00001619C:F12
244	10944	RTA00000126A.h.17.2	M00001549A:D08
245	39809	RTA00000190AF.e.3.1	M00003907D:A09
246	22085	RTA00000135A.e.5.2	M00001541A:F07
247	19255	RTA00000135A.m.18.1	M00001545A:C03
248	14311	RTA00000192AF.o.2.1	M00004203B:C12
249	8479	RTA00000189AF.j.22.1	M00003875C:G07
250		RTA00000189AF.j.23.1	M00003875D:D11
251	4193	RTA00000184AF.e.13.1	M00001549B:F06
252	22814	RTA00000184AF.h.14.1	M00001553D:D10
253	39563	RTA00000179AF.k.20.1	M00001402A:E08
254	39420	RTA00000134A.o.23.1	M00001537A:F12
255	11589	RTA00000177AF.b.17.4	M00001340D:F10
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SEQ ID NO:	Cluster ID	Sequence Name	Clone Name
256	4937	RTA00000191AF.p.21.1	M00004108A:E06
257	39412	RTA00000133A.k.17.1	M00001511A:H06
258	4837	RTA00000185AR.k.3.2	M00001597C:H02
259	13046	RTA00000193AF.h.19.1	M00004296C:H07
260	4141	RTA00000177AF.p.20.3	M00001361A:A05
261	38085	RTA00000123A.e.15.1	M00001531A:D01
262		RTA00000189AF.p.8.1	M00003891C:H09
263	11451	RTA00000192AF.p.17.1	M00004214C:H05
264	14507	RTA00000189AR.1.23.2	M00003879D:A02
265	40054	RTA00000180AF.p.10.1	M00001439C:F08
266	39423	RTA00000134A.k.22.1	M00001535A:F10
267	39453	RTA00000135A.g.11.1	M00001542A:E06
268	10751	RTA00000187AF.k.7.1	M00001679D:D03
269	10751	RTA00000187AF.k.6.1	M00001679D:D03
270	78091	RTA00000187AF.j.6.1	M00001679C:F01
271	39539	RTA00000127A.i.21.1	M00001555A:B02
272		RTA00000182AF.I.15.1	M00001487B:H06
273		RTA00000194AF.d.13.1	M00004896A:C07
274		RTA00000128A.c.20.1	M00001558A:H05
275	9283	RTA00000181AR.m.22.2	M00001455D:F09
276	39168	RTA00000121A.1.10.1	M00001507A:H05
277	39458	RTA00000126A.p.15.2	M00001552A:D11
278	14391	RTA00000177AF.m.17.3	M00001355B:G10
279	39195	RTA00000137A.c.16.1	M00001555A:C01
280	7212	RTA00000193AF.b.14.1	M00004230B:C07
281	4015	RTA00000136A.e.12.1	M00001549A:B02
282	12977	RTA00000189AF.j.19.1	M00003875B:F04
283		RTA00000178AF.m.13.1	M00001384B:A11
284	14391	RTA00000191AF.1.7.1	M00004081C:D12
285		RTA00000194AF.c.23.1	M00004691D:A05
286		RTA00000181AF.b.7.1	M00001443B:F01
287	8358	RTA00000183AF.i.5.1	M00001528B:H04
288	1267	RTA00000125A.o.5.1	M00001546A:G11
289		RTA00000189AF.f.7.1	M00003851B:D08
290	16347	RTA00000184AF.e.15.1	M00001549C:E06
291	7899	RTA00000193AF.a.17.1	M00004223B:D09
292	2379	RTA00000178AF.a.6.1	M00001361D:F08
293	39478	RTA00000133A.i.5.1	M00001471A:B01
294	39392	RTA00000134A.m.16.1	M00001536A:C08
295	5053	RTA00000184AF.o.12.1	M00001564A:B12
296	16999	RTA00000185AF.k.9.1	M00001598A:G03
297	39180	RTA00000126A.n.8.2	M00001551A:F05
298	1037	RTA00000121A.f.8.1	M00001470A:B10
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WO 99/339	982		PCT/US98/27610
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299	6867	RTA00000178AF.e.12.1	M00001370A:C09
300	10539	RTA00000183AF.a.24.1	M00001499B:A11
301	41633	RTA00000118A.g.16.1	M00001449A:B12
302	23218	RTA00000187AR.c.5.2	M00001662C:A09
303	39380	RTA00000129A.e.24.1	M00001587A:B11
304		RTA00000185AF.d.24.1	M00001582D:F05
305		RTA00000177AF.o.4.3	M00001358C:C06
306	6974	RTA00000184AF.a.15.1	M00001544B:B07
307		RTA00000185AF.g.11.1	M00001590B:F03
308	15855	RTA00000184AF.j.1.1	M00001556A:H01
309	84328	RTA00000118A.p.10.1	M00001452A:B04
310	10145	RTA00000120A.g.12.1	M00001465A:B11
311	39805	RTA00000177AF.c.21.3	M00001342B:E06
312		RTA00000187AF.h.23.1	M00001679A:F06
313	6298	RTA00000187AR.i.10.2	M00001679B:F01
314	14367	RTA00000187AF.e.8.1	M00001670C:H02
315		RTA00000193AF.c,22.1	M00004249D:G12
316	16921	RTA00000183AF.k.6.1	M00001534A:C04
317	1577	RTA00000184AF.i.23.1	M00001556A:F11
318	8773	RTA00000187AF.f.24.1	M00001675A:C09
319		RTA00000194AF.a.11.1	M00004461A:B09
320	39886	RTA00000178AF.j.24.1	M00001380D:B09
321	13532	RTA00000181AF.c.4.1	M00001445A:F05
322		RTA00000193AF.d.2.1	M00004251C:G07
323	5257	RTA00000192AF.f.3.1	M00004146C:C11
324	9061	RTA00000191AR.e.11.2	M00004031A:A12
325	19267	RTA00000186AF.1.12.1	M00001645A:C12
326	20212	RTA00000134A.1.22.1	M00001535A:C06
327	16653	RTA00000181AF.k.5.3	M00001453C:F06
328	16985	RTA00000177AF.h.10.1	M00001348B:G06
329	12977	RTA00000189AR.j.19.1	M00003875B:F04
330	9061	RTA00000191AR.e.11.3	M00004031A:A12
331		RTA00000194AR.a.10.2	M00004461A:B08
332	6468	RTA00000187AF.d.15.1	M00001669B:F02
333	16392	RTA00000192AF.l.1.1	M00004183C:D07
334	14627	RTA00000187AF.g.23.1	M00001677C:E10
335	6583	RTA00000179AF.d.13.1	M00001394A:F01
336	6806	RTA00000177AF.g.13.3	M00001346D:E03
337	9635	RTA00000137A.e.23.4	M00001557A:F01
338	68 9	RTA00000181AR.l.22.1	M00001454D:G03
339	4119	RTA00000183AF.k.16.1	M00001534C:A01
340	8952	RTA00000183AF.h.15.1	M00001518C:B11
341	2379	RTA00000192AF.p.8.1	M00004212B:C07
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WO 99/339	82		PCT/US98/27610
SEQ ID NO:	Cluster ID	Sequence Name	Clone Name
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343	21877	RTA00000189AF.b.21.1	M00003833A:E05
344	6874	RTA00000192AF.a.14.1	M00004111D:A08
345	6874	RTA00000189AF.e.9.1	M00003846B:D06
346	37285	RTA00000191AF.f.11.1	M00004035C:A07
347		RTA00000193AF.j.20.1	M00004327B:H04
348	76 74	RTA00000118A.g.9.1	M00001416A:H01
349	2797	RTA00000180AF.i.19.1	M00001429A:H04
350		RTA00000184AF.g.22.1	M00001552D:A01
351	7802	RTA00000185AF.n.5.1	M00001608A:B03
352	16921	RTA00000193AF.h.15.1	M00004295D:F12
353	11494	RTA00000192AF.j.6.1	M00004172C:D08
354	17062	RTA00000177AF.b.8.4	M00001340B:A06
355	16245	RTA00000177AF.k.9.3	M00001352A:E02
356	83103	RTA00000119A.e.24.2	M00001454A:A09
357	4309	RTA00000186AF.e.22.1	M00001624C:F01
358	13072	RTA00000181AR.m.5.2	M00001455B:E12
359	4059	RTA00000177AF.n.18.3	M00001357D:D11
360	5178	RTA00000178AF.n.10.1	M00001386C:B12
361	1120	RTA00000118A.p.15.3	M00001452A:D08
362	6420	RTA00000183AF.d.11.1	M00001504D:G06
363	13913	RTA00000186AF.e.6.1	M00001623D:F10
364		RTA00000192AF.c.2.1	M00004121B:G01
365	3956	RTA00000183AF.g.3.1	M00001512D:G09
366	14364	RTA00000183AF.g.12.1	M00001513C:E08
367	6880	RTA00000191AF.m.20.1	M00004087D:A01
368	84182	RTA00000180AF.h.19.1	M00001428A:H10
369	2790	RTA00000177AF.e.2.1	M00001343C:F10
370	4561	RTA00000184AF.i.21.1	M00001555D:G10
371	8847	RTA00000180AF.b.16.1	M00001416B:H11
372	56020	RTA00000193AF.g.2.1	M00004285B:E08
373	1531	RTA00000119A.o.3.1	M00001461A:D06
374	6420	RTA00000177AF.f.10.3	M00001345A:E01
375		RTA00000188AF.b.12.1	M00003754C:E09
376		RTA00000180AF.k.24.1	M00001432C:F06
377		RTA00000184AF.a.8.1	M00001544A:E06
378	2696	RTA00000134A.m.13.1	M00001536A:B07
379	260	RTA00000185AR.i.12.2	M00001594B:H04
380	11350	RTA00000189AF.a.24.2	M00003826B:A06
381	2428	RTA00000123A.l.21.1	M00001533A:C11
382	4313	RTA00000122A.n.3.1	M00001517A:B07
383		RTA00000184AF.p.3.1	M00001566B:D11
384	697	RTA00000188AF.d.6.1	M00003759B:B09
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386 4568 RTA00000122A.d.15.3 M00001513A:B06 387 RTA00000177AF.ic.62 M00001350A:B08 388 5622 RTA0000018AF.a.11.1 M00001362B:D10 389 7514 RTA00000184AF.k.21.1 M00000355B:H11 390 5619 RTA00000189AF.f.17.1 M00003853A:D04 391 7570 RTA00000189AF.c.21.1 M00003974D:E07 392 23358 RTA00000190AF.o.20.1 M00003974D:E07 394 5192 RTA00000184AF.k.2.1 M0000374D:E07 394 5192 RTA00000180AF.a.24.1 M00001415A:H06 396 RTA00000189AF.h.17.1 M00003857B:H10 397 RTA00000184AF.l.1.1 M00001559B:F01 398 RTA00000184AF.l.11.1 M00001559B:F01 399 4718 RTA00000184AF.l.1.1 M00001559B:F01 400 14929 RTA00000178AF.w.1.2 M00001353D:D10 401 4908 RTA00000178AF.k.16.1 M0000471D:B03 404 17732 RTA00000178AF.k.16.1 M00001340B:A06 405 </th <th></th> <th></th> <th>Sequence Name</th> <th>Clone Name</th>			Sequence Name	Clone Name
387 RTA00000177AF.i.6.2 M00001350A:B08 388 5622 RTA00000178AF.a.1l.1 M00001352B:D10 389 7514 RTA00000184AF.k.2l.1 M00001558B:H11 390 5619 RTA00000189AF.f.17.1 M000003853A:D04 391 7570 RTA00000187AF.g.24.1 M00001677D:A07 392 23358 RTA00000190AF.c.2l.1 M00003974D:H02 393 23210 RTA0000018AF.k.2.1 M00003974D:H02 394 5192 RTA0000018AF.k.2.1 M00001557B:H10 395 13538 RTA0000018AF.k.2.1 M00001557B:H10 396 RTA00000189AF.k.2.1 M00003867A:D10 397 RTA00000189AF.g.5.1 M00003867A:D10 398 RTA00000189AF.g.5.1 M00003857A:H03 400 14929 RTA00000189AF.g.5.1 M00001353D:D10 401 4908 RTA0000017AF.m.l.2 M00001353D:D10 402 RTA00000194AF.c.24.1 M0000492A:H08 403 RTA00000194AF.c.24.1 M0000492A:H08 404 17732 RTA000001	385	5619	RTA00000188AF.I.9.1	M00003796C:D05
388 5622 RTA00000178AF.a.11.1 M00001362B:D10 389 7514 RTA00000184AF.k.21.1 M00001558B:H11 390 5619 RTA00000187AF.g.24.1 M00001677D:A07 391 7570 RTA00000187AF.g.24.1 M00001677D:A07 392 23358 RTA00000190AF.o.20.1 M00003974D:E07 394 5192 RTA00000184AF.k.2.1 M00001557B:H10 395 13538 RTA00000184AF.a.24.1 M000014557B:H10 396 RTA00000189AF.h.24.1 M000014557B:H10 397 RTA00000189AF.h.17.1 M00003867A:D10 398 RTA00000184AF.I.1.1 M00001559B:F01 399 4718 RTA00000189AF.g.5.1 M00001353D:D6 400 14929 RTA0000017AF.m.1.2 M00001353D:D10 401 4908 RTA0000017AF.m.1.2 M0000133D:D6 403 RTA0000017AF.k.1.6.1 M0000134D:E06 403 RTA00000178AF.k.16.1 M00001340B:A06 404 17732 RTA00000178AF.k.22 M00001340B:A06 405 17062 </td <td>386</td> <td>4568</td> <td>RTA00000122A.d.15.3</td> <td>M00001513A:B06</td>	386	4568	RTA00000122A.d.15.3	M00001513A:B06
389 7514 RTA00000184AF.k.21.1 M00001558B:H11 390 5619 RTA00000187AF.g.24.1 M00003853A:D04 391 7570 RTA00000187AF.g.24.1 M0000167TD:A07 392 23358 RTA00000190AF.o.20.1 M00003974D:E07 394 5192 RTA00000180AF.a.24.1 M0000157B:H10 395 13538 RTA00000180AF.a.24.1 M00001457B:H10 396 RTA00000189AF.h.17.1 M00003867A:D10 397 RTA00000192AF.o.11.1 M00003867A:D10 398 RTA00000192AF.o.11.1 M00001559B:F01 399 4718 RTA00000189AF.g.5.1 M00003857A:H03 400 14929 RTA0000017AF.m.1.2 M00001353D:D10 401 4908 RTA00000178AF.k.16.1 M00001353D:D10 402 RTA00000178AF.k.16.1 M00001376B:G06 403 RTA00000178AF.k.16.1 M00001376B:G06 404 17732 RTA00000178AF.i.02.2 M00001340B:A06 405 17062 80.A1.sp6:130228.Seq M00001340B:A06 406 <td< td=""><td>387</td><td></td><td>RTA00000177AF.i.6.2</td><td>M00001350A:B08</td></td<>	387		RTA00000177AF.i.6.2	M00001350A:B08
390 5619 RTA00000189AF.f.17.1 M00003853A:D04 391 7570 RTA00000187AF.g.24.1 M00001677D:A07 392 23358 RTA00000190AF.o.21.1 M00003974D:H02 393 23210 RTA00000184AF.k.2.1 M00003974D:E07 394 5192 RTA00000184AF.k.2.1 M00001557B:H10 395 13538 RTA00000189AF.h.17.1 M00001415A:H06 396 RTA00000189AF.h.17.1 M000025D:F06 397 RTA00000184AF.I.11.1 M0000125D:F06 398 RTA00000184AF.I.11.1 M00001559B:F01 399 4718 RTA00000189AF.g.5.1 M000013857A:H03 400 14929 RTA00000178AF.g.5.1 M000013857A:H03 401 4908 RTA00000178AF.k.16.1 M00001381D:E06 403 RTA00000178AF.k.16.1 M00001381D:E06 404 17732 RTA00000178AF.k.22 M00001340B:A06 405 17062 30.A1.sp6:130228.Seq M00001340B:A06 406 11589 30.B1.sp6:130225.Seq M00001340B:A06 <td< td=""><td>388</td><td>5622</td><td>RTA00000178AF.a.11.1</td><td>M00001362B:D10</td></td<>	388	5622	RTA00000178AF.a.11.1	M00001362B:D10
391 7570 RTA00000187AF.g.24.1 M00001677D:A07 392 23358 RTA00000190AF.o.20.1 M00003974D:H02 393 23210 RTA00000190AF.o.20.1 M00003974D:E07 394 5192 RTA00000184AF.k.2.1 M00001557B:H10 395 13538 RTA00000189AF.h.17.1 M00001415A:H06 396 RTA00000192AF.o.11.1 M0000255D:F06 398 RTA00000192AF.g.5.1 M00003857A:H03 400 14929 RTA0000017AF.m.1.2 M00001559B:F01 399 4718 RTA0000017AF.m.1.2 M00001353D:D10 401 4908 RTA00000178AF.k.16.1 M00004171D:B03 402 RTA00000178AF.k.16.1 M00004171D:B03 403 RTA00000178AF.k.16.1 M0000134D:B06 404 17732 RTA00000178AF.k.16.1 M00001376B:G06 405 17062 80.A1.sp6:13028.Seq M00001340B:A06 406 11589 80.B1.sp6:130228.Seq M0000134D:F10 407 4443 80.C1.sp6:130232.Seq M00001342B:E06 40	389	7514	RTA00000184AF.k.21.1	M00001558B:H11
392 23358 RTA00000190AF.o.21.1 M00003974D:H02 393 23210 RTA00000190AF.o.20.1 M00003974D:E07 394 5192 RTA00000184AF.k.2.1 M00001557B:H10 395 13538 RTA00000180AF.a.24.1 M0000145A:H06 396 RTA00000192AF.o.11.1 M00003867A:D10 397 RTA00000192AF.o.11.1 M00004205D:F06 398 RTA00000180AF.g.5.1 M00001559B:F01 399 4718 RTA00000189AF.g.5.1 M00001353D:D10 400 14929 RTA00000178AF.in.1.2 M00001353D:D10 401 4908 RTA00000178AF.k.16.1 M00004171D:B03 402 RTA00000178AF.k.16.1 M0000131D:E06 403 RTA00000178AF.k.2.4.1 M0000439:B1:E06 404 17732 RTA00000178AF.c.24.1 M00001381D:E06 405 17062 80.A1.sp6:130220.Seq M0000134D:E10 406 11589 80.B1.sp6:130220.Seq M0000134D:E10 407 4443 80.C1.sp6:130223.Seq M00001342B:E06 409 <t< td=""><td>390</td><td>5619</td><td>RTA00000189AF.f.17.1</td><td>M00003853A:D04</td></t<>	390	5619	RTA00000189AF.f.17.1	M00003853A:D04
393 23210 RTA00000190AF.o.20.1 M00003974D:E07 394 5192 RTA00000184AF.k.2.1 M00001557B:H10 395 13538 RTA00000180AF.a.24.1 M00001415A:H06 396 RTA00000189AF.h.17.1 M000003867A:D10 397 RTA00000189AF.o.11.1 M00004205D:F06 398 RTA00000184AF.i.11.1 M00004559B:F01 399 4718 RTA00000189AF.g.5.1 M00003857A:H03 400 14929 RTA00000177AF.m.1.2 M00001353D:D10 401 4908 RTA00000178AF.k.16.1 M00004171D:B03 402 RTA00000178AF.k.16.1 M00004171D:B03 403 RTA00000178AF.i.2.2 M00001376B:G06 404 17732 RTA00000178AR.i.2.2 M00001376B:G06 405 17062 80.A1.sp6:130220.Seq M00001340B:A06 406 11589 80.B1.sp6:130220.Seq M00001341A:E12 408 39805 80.D1.sp6:130232.Seq M000013432B:B06 409 2790 80.E1.sp6:130256.Seq M000013454:E01 411	391	7570	RTA00000187AF.g.24.1	M00001677D:A07
394 5192 RTA00000184AF.k.2.1 M00001557B:H10 395 13538 RTA00000180AF.a.24.1 M00001415A:H06 396 RTA00000189AF.h.17.1 M00003867A:D10 397 RTA00000192AF.o.11.1 M00004205D:F06 398 RTA00000184AF.l.11.1 M00001559B:F01 399 4718 RTA00000189AF.g.5.1 M00001387A:H03 400 14929 RTA00000177AF.m.1.2 M00001353D:D10 401 4908 RTA00000178AF.k.16.1 M00004171D:B03 402 RTA00000178AF.k.16.1 M00001381D:E06 403 RTA00000178AF.k.16.1 M00001376B:G06 404 17732 RTA00000178AR.i.2.2 M00001376B:G06 405 17062 80.A1.sp6:130220.Seq M00001340B:A06 406 11589 80.B1.sp6:130220.Seq M00001340D:F10 407 4443 80.C1.sp6:130232.Seq M00001342B:E06 409 2790 80.E1.sp6:130244.Seq M000013432:F10 410 23255 80.F1.sp6:130258.Seq M00001345A:E01 412 <t< td=""><td>392</td><td>23358</td><td>RTA00000190AF.o.21.1</td><td>M00003974D:H02</td></t<>	392	23358	RTA00000190AF.o.21.1	M00003974D:H02
395 13538 RTA00000180AF.a.24.1 M00001415A:H06 396 RTA00000189AF.h.17.1 M00003867A:D10 397 RTA00000192AF.o.11.1 M00004205D:F06 398 RTA00000184AF.l.11.1 M00001559B:F01 399 4718 RTA00000189AF.g.5.1 M00003857A:H03 400 14929 RTA00000177AF.m.1.2 M0000135D:D10 401 4908 RTA00000192AF.j.2.1 M00004171D:B03 402 RTA00000194AF.k.16.1 M00004171D:B03 403 RTA00000194AF.c.24.1 M00004692A:H08 404 17732 RTA00000178AR.i.2.2 M00001376B:G06 405 17062 80.A1.sp6:130220.Seq M00001340B:A06 406 11589 80.B1.sp6:130223.Seq M0000134D:F10 407 4443 80.C1.sp6:130232.Seq M00001342B:E06 409 2790 80.E1.sp6:1302256.Seq M00001342B:E06 409 2790 80.E1.sp6:130280.Seq M00001343D:H07 411 6420 80.G1.sp6:130280.Seq M00001348D:H07 412	393	23210	RTA00000190AF.o.20.1	M00003974D:E07
396 RTA00000189AF.h.17.1 M00003867A:D10 397 RTA00000192AF.o.11.1 M00004205D:F06 398 RTA00000184AF.l.11.1 M00001559B:F01 399 4718 RTA00000189AF.g.5.1 M00003857A:H03 400 14929 RTA00000177AF.m.1.2 M00001353D:D10 401 4908 RTA00000192AF.j.2.1 M00001417ID:B03 402 RTA0000019AF.k.l.6.1 M0000181D:E06 403 RTA00000194AF.c.24.1 M00004692A:H08 404 17732 RTA00000178AR.i.2.2 M00001376B:G06 405 17062 80.A1.sp6:130220.Seq M00001340B:A06 406 11589 80.B1.sp6:130220.Seq M00001340B:A06 407 4443 80.C1.sp6:130232.Seq M00001340B:DE10 407 4443 80.C1.sp6:130232.Seq M000013432:E10 410 23255 80.F1.sp6:130256.Seq M000013432:F10 410 23255 80.F1.sp6:130268.Seq M00001343:E01 411 6420 80.G1.sp6:130280.Seq M00001340B:B04 412 <t< td=""><td>394</td><td>5192</td><td>RTA00000184AF.k.2.1</td><td>M00001557B:H10</td></t<>	394	5192	RTA00000184AF.k.2.1	M00001557B:H10
396 RTA00000189AF.h.17.1 M00003867A:D10 397 RTA00000192AF.o.11.1 M00004205D:F06 398 RTA00000184AF.l.11.1 M00001559B:F01 399 4718 RTA00000189AF.g.5.1 M00003857A:H03 400 14929 RTA00000177AF.m.1.2 M00001353D:D10 401 4908 RTA00000178AF.k.16.1 M0000181D:B03 402 RTA00000194AF.c.24.1 M00004692A:H08 403 RTA00000194AF.c.24.1 M00004692A:H08 404 17732 RTA00000178AR.i.2.2 M00001376B:G06 405 17062 80.A1.sp6:130220.Seq M00001340B:A06 406 11589 80.B1.sp6:130220.Seq M00001340B:A06 407 4443 80.C1.sp6:130232.Seq M00001340B:A06 408 39805 80.D1.sp6:130232.Seq M000013432E:E06 409 2790 80.E1.sp6:130256.Seq M000013432E:E0 410 23255 80.F1.sp6:130268.Seq M000013432E:E0 411 6420 80.G1.sp6:130280.Seq M00001347A:E01 412 <	395	13538	RTA00000180AF.a,24.1	M00001415A:H06
397 RTA00000192AF.o.11.1 M00004205D:F06 398 RTA00000184AF.l.11.1 M00001559B:F01 399 4718 RTA00000189AF.g.5.1 M00003857A:H03 400 14929 RTA00000177AF.m.1.2 M00001353D:D10 401 4908 RTA00000178AF.k.16.1 M0000417D:B03 402 RTA00000178AF.k.16.1 M00001381D:E06 403 RTA00000178AF.k.16.1 M000001376B:G06 404 17732 RTA00000178AR.i.2.2 M00001376B:G06 405 17062 80.A1.sp6:130208.Seq M00001340B:A06 406 11589 80.B1.sp6:130220.Seq M00001340D:F10 407 4443 80.C1.sp6:130232.Seq M00001342B:E06 409 2790 80.E1.sp6:130226.Seq M000013432E:F10 410 23255 80.F1.sp6:130280.Seq M00001343D:H07 411 6420 80.G1.sp6:130280.Seq M00001345A:E01 412 5007 80.H1.sp6:130292.Seq M00001345A:E01 413 13576 80.D2.sp6:130245.Seq M00001345A:E01	396		RTA00000189AF.h.17.1	M00003867A:D10
398 RTA00000184AF.I.11.1 M00001559B:F01 399 4718 RTA00000189AF.g.5.1 M00003857A:H03 400 14929 RTA00000177AF.m.1.2 M00001353D:D10 401 4908 RTA00000178AF.k.16.1 M00004171D:B03 402 RTA00000178AF.k.16.1 M00001381D:E06 403 RTA00000178AF.k.16.1 M00004692A:H08 404 17732 RTA00000178AR.i.2.2 M00001340B:G06 405 17062 80.A1.sp6:130220.Seq M00001340D:F10 406 11589 80.B1.sp6:130220.Seq M00001340D:F10 407 4443 80.C1.sp6:130232.Seq M00001341A:E12 408 39805 80.D1.sp6:130244.Seq M000013432:E06 409 2790 80.E1.sp6:130246.Seq M000013432:E06 410 23255 80.F1.sp6:130245.Seq M00001345A:E01 411 6420 80.G1.sp6:130280.Seq M00001345A:E01 412 5007 80.H1.sp6:130225.Seq M00001346A:F09 413 13576 80.D2.sp6:130280.Seq M00001349B:B04			RTA00000192AF.o.11.1	M00004205D:F06
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404 17732 RTA00000178AR.i.2.2 M00001376B:G06 405 17062 80.A1.sp6:130208.Seq M00001340B:A06 406 11589 80.B1.sp6:130220.Seq M00001340D:F10 407 4443 80.C1.sp6:130232.Seq M00001341A:E12 408 39805 80.D1.sp6:130244.Seq M00001342E:E06 409 2790 80.E1.sp6:130256.Seq M00001343C:F10 410 23255 80.F1.sp6:130268.Seq M00001343D:H07 411 6420 80.G1.sp6:130280.Seq M00001345A:E01 412 5007 80.H1.sp6:130292.Seq M00001346A:F09 413 13576 80.D2.sp6:130245.Seq M00001347A:B10 414 16927 80.E2.sp6:130257.Seq M00001348B:B04 415 16985 80.F2.sp6:130257.Seq M00001348B:G06 416 3584 80.G2.sp6:130281.Seq M00001349B:B08 417 80.H2.sp6:130293.Seq M00001349B:B08 418 7187 80.A3.sp6:130246.Seq M00001350A:H01 419 16245 80.D3.sp6:1302				
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426 945 80.E4.sp6:130259.Seq M00001362C:H11			•	
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721 40132 00.1 4.5p0.1302/1.5eq 19100001303C.C10			•	
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WO 99/3398	82		PCT/US98/27610
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429	6867	80.H4.sp6:130295.Seq	M00001370A:C09
430	7172	80.A5.sp6:130212.Seq	M00001371C:E09
431	17732	80.B5.sp6:130224.Seq	M00001376B:G06
432	39833	80.C5.sp6:130236.Seq	M00001378B:B02
433	1334	80.D5.sp6:130248.Seq	M00001379A:A05
434	39886	80.E5.sp6:130260.Seq	M00001380D:B09
435		80.F5.sp6:130272.Seq	M00001381D:E06
436	22979	80.G5.sp6:130284.Seq	M00001382C:A02
437	39648	80.H5.sp6:130296.Seq	M00001383A:C03
438		80.B6.sp6:130225.Seq	M00001384B:A11
439	5178	80.C6.sp6:130237.Seq	M00001386C:B12
440	2464	80.D6.sp6:130249.Seq	M00001387A:C05
441	7587	80.E6.sp6:130261.Seq	M00001387B:G03
442	5832	80.F6.sp6:130273.Seq	M00001388D:G05
443	16269	80.G6.sp6:130285.Seq	M00001389A:C08
444	6583	80.H6.sp6:130297.Seq	M00001394A:F01
445	4009	80.A7.sp6:130214.Seq	M00001396A:C03
446		80.B7.sp6:130226.Seq	M00001400B:H06
447	39563	80.C7.sp6:130238.Seq	M00001402A:E08
448	5556	80.D7.sp6:130250.Seq	M00001407B:D11
449	9577	80.E7.sp6:130262.Seq	M00001409C:D12
450	7005	80.F7.sp6:130274.Seq	M00001410A:D07
451	8551	80.G7.sp6:130286.Seq	M00001412B:B10
452		80.H7.sp6:130298.Seq	M00001414A:B01
453		80.A8.sp6:130215.Seq	M00001414C:A07
454	13538	80.B8.sp6:130227.Seq	M00001415A:H06
455	8847	80.C8.sp6:130239.Seq	M00001416B:H11
456	36393	80.D8.sp6:130251.Seq	M00001417A:E02
457	9952	80.E8.sp6:130263.Seq	M00001418B:F03
458	9577	80.G8.sp6:130287.Seq	M00001421C:F01
459	15066	80.H8.sp6:130299.Seq	M00001423B:E07
460	10470	80.A9.sp6:130216.Seq	M00001424B:G09
461	22195	80.B9.sp6:130228.Seq	M00001425B:H08
462		80.C9.sp6:130240.Seq	M00001426B:D12
463	4261	80.D9.sp6:130252.Seq	M00001426D:C08
464	84182	80.E9.sp6:130264.Seq	M00001428A:H10
46 5	40392	80.H9.sp6:130300.Seq	M00001429D:D07
466	16731	80.C10.sp6:130241.Seq	M00001442C:D07
467		80.D10.sp6:130253.Seq	M00001443B:F01
468	13532	80.E10.sp6:130265.Seq	M00001445A:F05
46 9	8	80.H10.sp6:130301.Seq	M00001448D:C09
470	36313	80.A11.sp6:130218.Seq	M00001448D:H01
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474	86110	80.E11.sp6:130266.Seq	M00001449C:D06
475	32663	80.F11.sp6:130278.Seq	M00001450A:A11
476	27250	80.G11.sp6:130290.Seq	M00001450A:D08
477	16970	80.H11.sp6:130302.Seq	M00001452C:B06
478	16130	80.A12.sp6:130219.Seq	M00001453A:E11
479	16653	80.B12.sp6:130231.Seq	M00001453C:F06
480	7005	80.C12.sp6:130243.Seq	M00001454B:C12
481	13072	80.F12.sp6:130279.Seq	M00001455B:E12
482	9283	80.G12.sp6:130291.Seq	M00001455D:F09
483	23255	100.C1.sp6:131446.Seq	M00001343D:H07
484	13576	100.E1.sp6:131470.Seq	M00001347A:B10
485	7187	100.C2.sp6:131447.Seq	M00001350A:H01
486	14391	100.E3.sp6:131472.Seq	M00001355B:G10
487	945	100.E4.sp6:131473.Seq	M00001362C:H11
488	7172	100.A5.sp6:131426.Seq	M00001371C:E09
489	39648	100.A6.sp6:131427.Seq	M00001383A:C03
490	84182	100.G9.sp6:131502.Seq	M00001428A:H10
491	8	100.B11.sp6:131444.Seq	M00001448D:C09
492	36535	100.D11.sp6:131468.Seq	M00001449A:G10
493	82498	100.F11.sp6:131492.Seq	M00001450A:B12
494	16970	100.C12.sp6:131457.Seq	M00001452C:B06
495	16130	100.D12.sp6:131469.Seq	M00001453A:E11
496	7005	121.D1.sp6:131917.Seq	M00001454B:C12
497		121.G6.sp6:131958.Seq	M00001506D:A09
498	18957	121.F7.sp6:131947.Seq	M00001528A:F09
499	40044	122.E1.sp6:132121.Seq	M00001621C:C08
500	5214	122.C2.sp6:132098.Seq	M00001630B:H09
501	6660	122.B5.sp6:132089.Seq	M00001679A:A06
502	13183	123.D5.sp6:132305.Seq	M00004114C:F11
503	6455	123.E7.sp6:132319.Seq	M00004157C:A09
504	5319	123.F7.sp6:132331.Seq	M00004169C:C12
505	11443	123.A8.sp6:132272.Seq	M00004185C:C03
506		123.C8.sp6:132296.Seq	M00004191D:B11
507	8210	123.E8.sp6:132320.Seq	M00004197D:H01
508	9457	123.D11.sp6:132311.Seq	M00004307C:A06
509	6420	172.E1.sp6:133925.Seq	M00001345A:E01
510	16245	172.D2.sp6:133914.Seq	M00001352A:E02
511	8078	172.C3.sp6:133903.Seq	M00001353A:G12
512	14929	172.D3.sp6:133915.Seq	M00001353D:D10
513	14391	172.H3.sp6:133963.Seq	M00001355B:G10
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516		172.B9.sp6:133897.Seq	M00001400B:H06
517		176.A3.sp6:134514.Seq	M00001632D:H07
518	19267	176.G3.sp6:134586.Seq	M00001645A:C12
519	78091	176.G5.sp6:134588.Seq	M00001679C:F01
520	17055	176.D6.sp6:134553.Seq	M00001682C:B12
521	6539	176.D9.sp6:134556.Seq	M00003844C:B11
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523	5257	177.F5.sp6:134768.Seq	M00004146C:C11
524	11494	177.E6.sp6:134757.Seq	M00004172C:D08
525		177.G7.sp6:134782.Seq	M00004205D:F06
526	11451	177.D8.sp6:134747.Seq	M00004214C:H05
527	9283	173.D2.SP6:134106.Seq	M00001455D:F09
528	16283	173.F3.SP6:134131.Seq	M00001467A:D08
529	10539	173.B5.SP6:134085.Seq	M00001499B:A11
530	6420	173.F5.SP6:134133.Seq	M00001504D:G06
531	3956	173.H5.SP6:134157.Seq	M00001512D:G09
532		173.G7.SP6:134147.Seq	M00001544A:E06
533	1577	173.C9.SP6:134101.Seq	M00001556A:F11
534	9635	173.D9.SP6:134113.Seq	M00001557A:F01
535	5192	173.E9.SP6:134125.Seq	M00001557B:H10
536	6539	173.A12.SP6:134080.Seq	M00001579D:C03
537	945	180.C2.sp6:135940.Seq	M00001362C:H11
538	7005	180.H5.sp6:136003.Seq	M00001410A:D07
539	39304	180.G9.sp6:135995.Seq	M00001450A:A02
540	27250	180.B10.sp6:135936.Seq	M00001450A:D08
541	35555	184.A5.sp6:135530.Seq	M00001528A:C04
542	19255	184.B10.sp6:135547.Seq	M00001545A:C03
543	6268	184.C12.sp6:135561.Seq	M00001551A:B10
544	3277	217.E1.sp6:139406.Seq	M00001624A:B06
545	39171	217.A12.sp6:139369.Seq	M00001644C:B07
546	11460	219.F2.sp6:139035.Seq	M00001676B:F05
547	10539	219.F6.sp6:139039.Seq	M00001680D:F08
548	11476	219.H8.sp6:139065.Seq	M00003747D:C05
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550	7674	79.C1.sp6:130040.Seq	M00001416A:H01
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552	39304	79.F1.sp6:130076.Seq	M00001450A:A02
553	82498	79.G1.sp6:130088.Seq	M00001450A:B12
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560	16283	79.H3.sp6:130102.Seq	M00001467A:D08
561	4568	79.D4.sp6:130055.Seq	M00001513A:B06
562	4313	79.F4.sp6:130079.Seq	M00001517A:B07
563	2428	79.A5.sp6:130020.Seq	M00001533A:C11
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571	39180	79.A7.sp6:130022.Seq	M00001551A:F05
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574	39490	79.G7.sp6:130094.Seq	M00001557A:F03
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576	39380	79.E8.sp6:130071.Seq	M00001587A:B11
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587	39442	89.A2.sp6:130668.Seq	M00001467A:E10
588	7589	89.B2.sp6:130680.Seq	M00001468A:F05
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590	12081	89.D2.sp6:130704.Seq	M00001469A;C10
591	19105	89.E2.sp6:130716.Seq	M00001469A;H12
592	1037	89.F2.sp6:130728.Seq	M00001470A:B10
593	39425	89.G2.sp6:130740.Seq	M00001470A:C04
594	39478	89.H2.sp6:130752.Seq	M00001471A:B01
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598	7206	89.E3.sp6:130717.Seq	M00001490B:C04 M00001494D:F06
599	2623	89.F3.sp6:130729.Seq	M00001497A:G02
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604	9685	89.C4.sp6:130694.Seq	M00001501D:C02
605		89.D4.sp6:130706.Seq	M00001504A:E01
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646	5175	89.C10.sp6:130700.Seq	M00001551A:G06
647	22390	89.D10.sp6:130712.Seq	M00001551C:G09
648	3266	89.E10.sp6:130724.Seq	M00001552B:D04
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658	1577	89.F11.sp6:130737.Seq	M00001556B:C08
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690		90.E4.sp6:130910.Seq	M00001632D:H07
691	39171	90.F4.sp6:130922.Seq	M00001644C:B07
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696	76760	90.C5.sp6:130887.Seq	M00001657D:F08
697	23218	90.D5.sp6:130899.Seq	M00001662C:A09
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700	14367	90.G5.sp6:130935.Seq	M00001670C:H02
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704	7570	90.D6.sp6:130900.Seq	M00001677D:A07
705	4416	90.E6.sp6:130912.Seq	M00001678D:F12
706	6660	90.F6.sp6:130924.Seq	M00001679A:A06
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727	7899	90.H9.sp6:130951.Seq	M00003837D:A01
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756	40122	99.D2.sp6:131267.Seq	M00003970C:B09
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775	13183	99.G5.sp6:131306.Seq	M00004114C:F11
776		99.H5.sp6:131318.Seq	M00004121B:G01
777	13272	99.A6.sp6:131235.Seq	M00004138B:H02
778	5257	99.B6.sp6:131247.Seq	M00004146C:C11
779	6455	99.D6.sp6:131271.Seq	M00004157C:A09
780	5319	99.E6.sp6:131283.Seq	M00004169C:C12
781	4908	99.F6.sp6:131295.Seq	M00004171D:B03
782	11494	99.G6.sp6:131307.Seq	M00004172C:D08
783	11443	99.A7.sp6:131236.Seq	M00004185C:C03
784		99.B7.sp6:131248.Seq	M00004191D:B11
785	8210	99.C7.sp6:131260.Seq	M00004197D:H01
786	14311	99.D7.sp6:131272.Seq	M00004203B:C12
787		99.E7.sp6:131284.Seq	M00004205D:F06
788	12971	99.B8.sp6:131249.Seq	M00004223D:E04
789	6455	99.C8.sp6:131261.Seq	M00004229B:F08
790	7212	99.D8.sp6:131273.Seq	M00004230B:C07
791	4905	99.H8.sp6:131321.Seq	M00004269D:D06
792	16914	99.A9.sp6:131238.Seq	M00004275C:C11
79 3	16921	99.D9.sp6:131274.Seq	M00004295D:F12
794	13046	99.E9.sp6:131286.Seq	M00004296C:H07
79 5	9457	99.F9.sp6:131298.Seq	M00004307C:A06
796	26295	99.G9.sp6:131310.Seq	M00004312A:G03
797	21847	99.H9.sp6:131322.Seq	M00004318C:D10
798		99.H10.sp6:131323.Seq	M00004505D:F08
799		99.B11.sp6:131252.Seq	M00004692A:H08
800		99.D11.sp6:131276.Seq	M00005180C:G03
801	39304	RTA00000118A.j.21.1.Seq_THC151859	
802	2428	RTA00000123A.l.21.1.Seq_THC205063	
803	1058	RTA00000126A.e.20.3.Seq_THC217534	
804	5097	RTA00000134A.k.1.1.Seq_THC215869	
805	20212	RTA00000134A.I.22.1.Seq_THC128232	
806	23255	RTA00000177AF.e.14.3.Seq_THC228776	
807	2790	RTA00000177AF.e.2.1.Seq_THC229461	
808	6420	RTA00000177AF.f.10.3.Seq_THC226443	
809	4059	RTA00000177AF.n.18.3.Seq_THC123051	
810		RTA00000179AF.j.13.1.Seq_THC105720	
811	9952	RTA00000180AF.c.20.1.Seq_THC162284	
812	13238	RTA00000181AF.m.4.1.Seq_THC140691	
813	9685	RTA00000183AF.c.11.1.Seq_THC109544	
814		RTA00000183AF.c.24.1.Seq_THC125912	
		1.50	

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SEQ ID NO:	Cluster ID	Sequence Name	Clone Name
815	6420	RTA00000183AF.d.11.1.Seq_THC226443	
816	6974	RTA00000183AF.d.9.1.Seq_THC223129	
817	40044	RTA00000183AF.g.22.1.Seq_THC232899	
818		RTA00000183AF.g.9.1.Seq_THC198280	
819	5892	RTA00000184AF.d.11.1.Seq_THC161896	
820	40044	RTA00000186AF.d.1.1.Seq_THC232899	
821		RTA00000186AF.h.14.1.Seq_THC112525	
822	19267	RTA00000186AF.I.12.1.Seq_THC178183	
823	8773	RTA00000187AF.f.24.1.Seq_THC220002	
824	7570	RTA00000187AF.g.24.1.Seq_THC168636	
825	11476	RTA00000187AF.p.19.1.Seq_THC108482	
826		RTA00000188AF.d.11.1.Seq_THC212094	
827	17076	RTA00000188AF.d.21.1.Seq_THC208760	
828	697	RTA00000188AF.d.6.1.Seq_THC178884	
829	67907	RTA00000188AF.g.11.1.Seq_THC123222	
830	5619	RTA00000188AF.1.9.1.Seq_THC167845	
831	4718	RTA00000189AF.g.5.1.Seq_THC196102	
832	39809	RTA00000190AF.e.3.1.Seq_THC150217	
833	23255	RTA00000190AF.j.4.1.Seq_THC228776	
834	40122	RTA00000190AF.n.23.1.Seq_THC109227	
835	23210	RTA00000190AF.o.20.1.Seq_THC207240	
836	23358	RTA00000190AF.o.21.1.Seq_THC207240	
837	5693	RTA00000190AF.p.17.2.Seq_THC173318	
838	2433	RTA00000191AF.a.15.2.Seq_THC79498	
839	5257	RTA00000192AF.f.3.1.Seq_THC213833	
840	16392	RTA00000192AF.l.1.1.Seq_THC202071	
841		RTA00000193AF.c.21.1.Seq_THC222602	
842	26295	RTA00000193AF.i.24.2.Seq_THC197345	
843		RTA00000193AF.m.5.1.Seq_THC173318	
844		RTA00000193AF.n.15.1.Seq_THC215687	

Table 2

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant		
SEQ	ACCESSION	DESCRIPTION	P	Proteins) ACCESSION	DESCRIPTION	P
ID			VALUE			VALUE
1	<none></none>	<none></none>	<none></none>	<none></none>	<none></none>	<none></none>
2	<none></none>	<none></none>	<none></none>	<none></none>	<none></none>	<none></none>
3	<none></none>	<none></none>	<none></none>	<none></none>	<none></none>	<none></none>
4	<none></none>	<none></none>	<none></none>	BAR3_CHITE	PROTEIN 3 PRECURSOR>PIR2:S 08167 Balbiani ring 3 protein - midge (Chironomus tentans)>GP:CTBR3_1 C;tentans balbiani ring 3 (BR3) gene	1
5	<none></none>	<none></none>		CYAA_PODA N	CYCLASE (EC 4.6.1.1) (ATP PYROPHOSPHATE- LYASE) (ADENYLYL CYCLASE)>PIR2:JC4 747 adenylate cyclase (EC 4.6.1.1) - Podospora anserina>GP:PANADC Y_1 Podospora anserina adenyl cyclase gene, exons 1-4	1
6	<none></none>	<none></none>	<none></none>			0.97

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	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
7	<none></none>	<none></none>	<none></none>	ATFCA2_18	Arabidopsis thaliana DNA chromosome 4, ESSA I contig fragment No; 2; Hydroxyproline-rich glycoprotein homolog; Similarity to hydroxyproline-rich glycoprotein precursor- common tobacco	0.93
8	<none></none>	<none></none>	<none></none>	DHAL_ASPN G	ALDEHYDE DEHYDROGENASE (EC 1.2.1.3) (ALDDH)>GP:ASNA LDAA_1 Aspergillus niger aldehyde dehydrogenase (aldA) gene, complete cds	0.9
9	<none></none>	<none></none>	<none></none>	_	Neurospora crassa two- component histidine kinase (nik-1) gene, 5' region and partial cds	0.86
10	<none></none>	<none></none>	<none></none>	NEUG_BOVI N	NEUROGRANIN (P17) (B-50 IMMUNOREACTIVE C-KINASE SUBSTRATE) (BICKS) (FRAGMENT)>PIR2: A39034 neurogranin - bovine (fragment)	0.82
11	<none></none>	<none></none>		HUMBYSTIN _1	Homo sapiens bystin mRNA, complete cds	0.81
12	<none></none>	<none></none>	<none></none>	BTBMP1_1	Bos taurus BMP1 gene, partial sequence; Bone morphogenetic protein 1	0.69
13	<none></none>	<none></none>		TCCYSPROT _1	T;congolense mRNA for (prepro) cysteine proteinase	0.56
14	<none></none>	<none></none>	<none></none>	P60_LISIV	PROTEIN P60 PRECURSOR (INVASION- ASSOCIATED PROTEIN)>GP:LISIA PRELB_1 Listeria	0.15

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
					ivanovii extracellular protein homologue (iap) gene, complete cds	
15	<none></none>	<none></none>	<none></none>	HEX_ADE31	HEXON PROTEIN (LATE PROTEIN 2) (FRAGMENT)>PIR2: S37217 hexon protein - human adenovirus 31 (fragment)>GP:HSAT3 1H_1 H;sapiens adenovirus type 31 hexon gene; Hexon protein; Internal fragment containing hypervariable regions	0.15
16	<none></none>	<none></none>	<none></none>	HSU77493_1	Human Notch2 mRNA, partial cds; Transmembrane protein; hN	0.13
17	<none></none>	<none></none>	<none></none>	CYB_PARTE	(EC 1.10.2.2)>PIR2:S07743 cytochrome b - Paramecium tetraurelia mitochondrion (SGC6)>GP:MIPAGE N_19 Paramecium aurelia mitochondrial complete genome; Apocytochrome b (AA 1-391)	0.078
18	<none></none>	<none></none>	<none></none>	HUMERB27_ 1	Human c-erbB-2 gene, exon 7; C-erb-2 protein	0.054
19	<none></none>	<none></none>	<none></none>	DMTRXIII_2	D;melanogaster DNA for trxI and trxII genes; Trithorax protein trxI; Trithorax; putative>GP:DMTTHO RAX_2 D;melanogaster DNA for (putative) trithorax protein; Predicted trithorax protein	0.047

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	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant Proteins)			
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE	
20	<none></none>	<none></none>	<none></none>	CELB0281_5	Caenorhabditis elegans cosmid B0281; Similar to reverse transcriptases	0.043	
21	<none></none>	<none></none>	<none></none>	MOTY_VIBP A	SODIUM-TYPE FLAGELLAR PROTEIN MOTY PRECURSOR>GP:VP U06949_4 Vibrio parahaemolyticus BB22 RNase T (rnt) gene and flagellar motor component (moty) gene, complete cds	0.041	
22	<none></none>	<none></none>	<none></none>	A56263	beta-galactosidase (EC 3.2.1.23) isozyme 12 - Arthrobacter sp. (strain B7)>GP:ASU17417_1 Arthrobacter sp; beta-galactosidase gene, complete cds	0.04	
23	<none></none>	<none></none>	<none></none>	GSA_PSEAE	GLUTAMATE-1- SEMIALDEHYDE 2,1-AMINOMUTASE (EC 5.4.3.8) (GSA) (GLUTAMATE-1- SEMIALDEHYDE AMINOTRANSFERA SE) (GSA- AT)>PIR2:S57898 glutamate 1- semialdehyde 2,1- aminomutase - Pseudomonas aeruginosa>GP:PAHE ML_1 P;aeruginosa hemL gene; Glutamate 1-sem	0.038	
24	<none></none>	<none></none>	<none></none>	S16323	hypothetical protein - Arabidopsis thaliana>GP:ATHB1_1 A;thaliana homeobox gene Athb-1 mRNA; Open reading frame	0.035	

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	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant Proteins)		
SEQ	ACCESSION	DESCRIPTION	P	ACCESSION	DESCRIPTION	P
25 25	<none></none>	<none></none>	<none></none>	IRS1_RAT	INSULIN RECEPTOR SUBSTRATE- 1>PIR2:S16948 hypothetical protein IRS-1 - rat>GP:RNIRS1IRM_1 R;Norvegicus IRS-1 mRNA for insulin- receptor; During insulin stimulation, undergoes tyrosine phosphorylation and binds phosphatidylinositol 3-	0.027
26	<none></none>	<none></none>	<none></none>	CEM02G9_2	kinase Caenorhabditis elegans cosmid M02G9; M02G9;1; Similar to keratin like protein; cDNA EST yk308g11;5 comes from this gene; cDNA EST yk208e11;5 comes from this gene; cDNA EST yk208e11;3 comes	0.0088
27	<none></none>	<none></none>	<none></none>	S75490 <u></u> 3	competence region: iga=IgA protease, comA=transformation competence [Neisseria gonorrhoeae, MS11, Genomic, 3 genes, 2664 nt]	0.0041
28	<none></none>	<none></none>	<none></none>	EXTN_TOBA C	EXTENSIN PRECURSOR (CELL WALL HYDROXYPROLINE- RICH GLYCOPROTEIN)>PI R2:S06733 hydroxyproline-rich glycoprotein precursor - common tobacco>GP:NTEXT_1 Tobacco HRGPnt3 gene for extensin; Extensin (AA 1-620)	0.0025

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
29	<none></none>	<none></none>	<none></none>	HPCEGS_1	Hepatitis C virus complete genome sequence; Polyprotein	0.0014
30	<none></none>	<none></none>	<none></none>	HHVBC_4	Human hepatitis virus (genotype C, HMA) preS1, preS2, S, C, X, antigens, core antigen, X protein and polymerase	0.00093
31	<none></none>	<none></none>		HSLTGFBP4_ 1	Homo sapiens mRNA for latent transforming growth factor-beta binding protein-4; Latent TGF-beta binding protein-4	0.00061
32	<none></none>	<none></none>	<none></none>	S74909	transposase - Synechocystis sp. (PCC 6803)>GP:D90909_10 8 Synechocystis sp; PCC6803 complete genome, 11/27, 1311235- 1430418; Transposase; ORF_ID:slr2062	0.00051
33	<none></none>	<none></none>	<none></none>	GRN_MOUS E	GRANULINS PRECURSOR (ACROGRANIN)>GP: MUSAP_1 Mouse gene for acrogranin precursor, complete cds	0.00022
34	<none></none>	<none></none>		Ē	PROCOLLAGEN ALPHA 2(I) CHAIN PRECURSOR>PIR2:A 43291 collagen alpha 2(I) chain precursor - mouse>GP:MMCOL1 A2_1 Mouse COL1A2 mRNA for pro-alpha- 2(I) collagen	0.00016
35	<none></none>	<none></none>	<none></none>	MMMHC29N 7_2	Mus musculus major histocompatibility locus class III region:butyrophilin-like protein gene, partial cds; Notch4, PBX2, RAGE, lysophatidic acid acyl transferase-	8.00E-05

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant Proteins)			
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE	
					alpha, palmitoyl-		
36	<none></none>	<none></none>	<none></none>	NFH_RAT	NEUROFILAMENT TRIPLET H PROTEIN (200 KD NEUROFILAMENT PROTEIN) (NF-H) (FRAGMENT)	2.40E-05	
37	<none></none>	<none></none>	<none></none>	HUMVWFM_ I	Human von Willebrand factor mRNA, 3' end; Von Willebrand factor prepropeptide	1.70E-05	
38	<none></none>	<none></none>	<none></none>	CGHU2E	collagen alpha 2(XI) chain - human (fragment)	2.00E-06	
39	<none></none>	<none></none>	<none></none>	A61183	hypothetical protein (sdsB region) - Pseudomonas sp.	4.90E-08	
40	<none></none>	<none></none>	<none></none>	YM8L_YEAS T	HYPOTHETICAL 71.1 KD PROTEIN IN DSK2-CAT8 INTERGENIC REGION>PIR2:S5458 5 hypothetical protein YMR278w - yeast (Saccharomyces cerevisiae)>GP:SC802 1X_4 S;cerevisiae chromosome XIII cosmid 8021; Unknown; YM8021;04, unknown, len: 622, CAI: 0;16,	1.50E-09	
41	<none></none>	<none></none>	<none></none>	MTCY210_31	Mycobacterium tuberculosis cosmid Y210; Unknown; MTCY210;31, unknown, len: 299 aa, slight similarity to carboxykinases	3.10E-10	

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	Nearest			Nearest		
	Neighbor			Neighbor		
	(BlastN vs.			(BlastX vs.		
	Genbank)			Non-		1
				Redundant		
				Proteins)		
SEQ	ACCESSION	DESCRIPTION	P	ACCESSION	DESCRIPTION	P
ID			VALUE			VALUE
42	<none></none>	<none></none>	<none></none>	CEC01G10_5	Caenorhabditis elegans cosmid C01G10, complete sequence; C01G10;8; CDNA EST	2.30E-12
					CEMSC45R comes from this gene>GP:CEC01G10	
	:				5 Caenorhabditis elegans cosmid	
					C01G10; C01G10;8; CDNA EST CEMSC45R comes	
					from this gene	
43	<none></none>	<none></none>	<none></none>	HSU15779_1	Human p70 (ST5) mRNA, alternatively	9.50E-14
					spliced, complete cds; Differentially	
					expressed; alternatively spliced	
44	<none></none>	<none></none>	<none></none>	MTCY210 31	Mycobacterium	1.70E-17
				_	tuberculosis cosmid	
					Y210; Unknown;	
					MTCY210;31,	
					unknown, len: 299 aa,	I
					slight similarity to	İ
					carboxykinases	
45	U61403	Dictyostelium	1	U93472 1	Danio rerio PPARB	0.95
		discoideum PrlA		_	gene, partial cds;	
		(prlA) mRNA,			Nuclear receptor C	
		partial cds.			domain	
46	Z92832	Caenorhabditis	1	U93472 1	Danio rerio PPARB	0.94
		elegans DNA ***		_	gene, partial cds;	
		SEQUENCING			Nuclear receptor C	
		IN PROGRESS			domain	
		*** from clone				
		F31D4; HTGS				
		phase 1.				
47	L36557	Oryza sativa	1	HSU61262_1	Human neogenin	0.89
		(clone pRG3)		_	mRNA, complete cds	
		repetitive			•	
		element.				
				L	<u> </u>	

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	Nearest			Nearest		
	Neighbor			Neighbor		
	(BlastN vs.			(BlastX vs.		
	Genbank)			Non-		
				Redundant		
				Proteins)		
SEQ	ACCESSION	DESCRIPTION	P	ACCESSION	DESCRIPTION	P
ID I			VALUE			VALUE
48	AF005898	Homo sapiens	1	LRP1 CHICK	LOW-DENSITY	0.85
		Na,K-ATPase	_		LIPOPROTEIN	
		beta-3 subunit			RECEPTOR-	
		pseudogene,			RELATED PROTEIN	
		complete			1 PRECURSOR (LRP)	
		sequence.			(ALPHA-2-	
					MACROGLOBULIN	
					RECEPTOR)	
					(A2MR)>PIR2:A53102	
					LDL receptor-related	
					protein / alpha-2-	
					macroglobulin receptor	
					precursor -	
					chicken>GP:GGLRPA	
					2MR_1 G;gallus	
					mRNA for LRP/alp	
49	U18795	Saccharomyces	1	NKC1_SQUA	BUMETANIDE-	0.73
		cerevisiae		C	SENSITIVE SODIUM-	
		chromosome V			(POTASSIUM)-	
		cosmids 9669,			CHLORIDE	
		8334, 8199, and			COTRANSPORTER 2	
		lambda clone			(NA-K-CL	
		1160.			SYMPORTER)>PIR2:	
					A53491 bumetanide-	
					sensitive Na-K-C1	
					cotransporter - spiny	
					dogfish>GP:SANKCC	
					1_1 Squalus acanthias	
					bumetanide-sensitive	
					Na-K-Cl cotransport	
<u> </u>	4.0000505			DVDV OV SS	protein (NKCC	0.71
50	AC002523	Homo sapiens;	1	BXEN_CLOB		0.71
		HTGS phase 1,		О	NEUROTOXIN TYPE	
		54 unordered			E, NONTOXIC	
		pieces.			COMPONENT>GP:C	
					LOENT120_1	
					C;botulinum gene for	
					nontoxic component of	
					progenitor toxin,	
	L				complete cds	

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	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non-			
				Redundant Proteins)			
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE	
51	AC002345	***	1	P3K2 DICDI	PHOSPHATIDYLINO	0.58	
		SEQUENCING IN PROGRESS *** Genomic sequence from Human 17; HTGS phase 1, 10 unordered pieces.			SITOL 3-KINASE 2 (EC 2.7.1.137) (PI3-KINASE) (PTDINS-3-KINASE) (PI3K)>GP:DDU23477 1 Dictyostelium discoideum phosphatidylinositol- 4,5-diphosphate 3- kinase (PIK2) mRNA, complete cds		
52	X14253	Human mRNA for cripto protein.	1	155651	noradrenaline transporter - bovine>GP:BTU09198 _1 Bos taurus noradrenaline transporter mRNA, complete cds	0.55	
53	U23516	Caenorhabditis elegans cosmid B0416.	1	I69024	MHC sex-limited protein - mouse (fragment)>GP:MUSM HC4AD_1 Mouse class III H2-Slp sex-limited protein gene, exons 1, 2 and 3; MHC sex- limited protein	0.47	
54	AB006698	Arabidopsis thaliana genomic DNA, chromosome 5, P1 clone: MCL19.	1	S81293_1	L1 {insertion sequence, provirus} [human papillomavirus type 6b HPV6b, KP4, Genomic Mutant, 121 nt]; Authors note this reading frame results from a 454 bp deletion and resulting	0.25	
55	K03458	Human immunodeficienc y virus type 1, isolate Zaire 6, vif, tat, rev, env, nef genes and 3' LTR.	1	S13383	hydroxyproline-rich glycoprotein - sorghum	0.24	

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	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
56	B26794	T1016TR TAMU Arabidopsis thaliana genomic clone T1016.	1	RK34_PORP U	CHLOROPLAST 50S RIBOSOMAL PROTEIN L34>PIR2:S73111 ribosomal protein L34 - red alga (Porphyra purpurea) chloroplast>GP:PPU38 804_4 Porphyra purpurea chloroplast genome, complete sequence; 50S ribosomal protein L34	0.021
57	Z98950	Human DNA sequence *** SEQUENCING IN PROGRESS *** from clone 507115; HTGS phase 1.	1	D41132	collagen-related protein 4 - Hydra magnipapillata (fragment)>PIR2:S219 32 mini-collagen - Hydra sp.>GP:HSNCOL4_1 Hydra N-COL 4 mRNA for mini- collagen; No start codon	0.02
58	U57057	Human WD protein IR10 mRNA, complete cds.	1	DMU15602_1	l	0.019
59	U57057	Human WD protein IR10 mRNA, complete cds.	1	CR2_MOUSE	COMPLEMENT RECEPTOR TYPE 2 PRECURSOR (CR2) (COMPLEMENT C3D RECEPTOR)>PIR2:A4 3526 complement C3d/Epstein-Barr virus receptor 2 precursor - mouse>GP:MUSCR2A A_1 Murine complement receptor type 2 (CR2) mRNA, complete cds; Complement receptor type	0.0074

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	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
60	В65337	CIT-HSP- 2021H21.TF CIT-HSP Homo sapiens genomic clone 2021H21.	1	A38096	perlecan precursor - human>GP:HUMHSP G2B_1 Human heparan sulfate proteoglycan (HSPG2) mRNA, complete cds	0.0051
61	U84722	Human vascular endothelial cadherin mRNA, complete cds.	1	_	H;sapiens mRNA for TAFII135; Subunit of RNA polymerase II transcription factor TFIID	0.0012
62	L41493	Avian rotavirus (strain turkey 1) genomic segment 4 outer capsid protein (VP8*) gene.	I	Y328_MYCP N	HYPOTHETICAL PROTEIN MG328 HOMOLOG>PIR2:S73 693 MG328 homolog P01_orf1033 - Mycoplasma pneumoniae (ATCC 29342) (SGC3)>GP:MPAE000 035_2 Mycoplasma pneumoniae from bases 442306 to 452472 (section 35 of 63) of the complete genome; MG328 homolog,	0.00015
63	D63139	Aeromonas sp. gene for chitinase, complete and partial cds.	1	MTCY16B7_3	Mycobacterium tuberculosis cosmid SCY16B7; Unknown; MTCY16B7;03, initiation factor, len: 900, similar at C- terminal half to eg IF2_BACSU P17889 initiation factor if-2 (716 aa), fasta	6.30E-05

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	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
64	J04974	Human alpha-2 type XI collagen mRNA (COL11A2).	1	GDF6_BOVI N	GROWTH/DIFFEREN TIATION FACTOR GDF-6 PRECURSOR (CARTILAGE- DERIVED MORPHOGENETIC PROTEIN 2) (CDMP- 2) (FRAGMENT)>PIR2: B55452 cartilage- derived morphogenetic protein 2 precursor - bovine (fragment)>GP:BTU13 661 1 Bos taurus	1.00E-05
65	AC002394	Homo sapiens Chromosome 16 BAC clone CIT987-SKA- 211C6 ~complete genomic sequence, complete sequence.	1	CELC14F11_ 6	cartilage-derived morp Caenorhabditis elegans cosmid C14F11; Similar to aspartate aminotransferase; coded for by C; elegans cDNA CEMSF95FB; coded for by C; elegans cDNA yk41e4;3; coded for by C; elegans	4.60E-06
66	AB002312	Human mRNA for KIAA0314 gene, partial cds.	1	NATI_YEAS T	N-TERMINAL ACETYLTRANSFER ASE 1 (EC 2.3.1.88) (AMINO-TERMINAL, ALPHA- AMINO, ACETYLTRANSFER ASE 1)	1.00E-09
67	AC003085	Human BAC clone RG094H21 from 7q21-q22, complete sequence.	1	DP19_CAEEL	DPY-19 PROTEIN>PIR2:S446 29 f22b7.10 protein - Caenorhabditis elegans>GP:CELF22B 7_9 C;aenorhabditis elegans (Bristol N2) cosmid F22B7; Putative	4.20E-11
68		P.anserina complete mitochondrial genome.	177	NATI_YEAS T	N-TERMINAL ACETYLTRANSFER ASE 1 (EC 2.3.1.88) (AMINO-TERMINAL, ALPHA- AMINO, ACETYLTRANSFER	8.40E-12

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7	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant Proteins)			
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE	
					ASE 1)		
69	Z95399	Caenorhabditis elegans DNA *** SEQUENCING IN PROGRESS *** from clone Y39B6; HTGS phase 1.	1	CER06B9_5	Caenorhabditis elegans cosmid R06B9, complete sequence; R06B9;b; Protein predicted using Genefinder; preliminary prediction	1.50E-24	
70	AC002339	Arabidopsis thaliana chromosome II BAC T11A07 genomic sequence, complete sequence.	0.99	POLG_BVDV S	GENOME POLYPROTEIN>PIR1 :A44217 genome polyprotein - bovine viral diarrhea virus (strain SD- 1)>GP:BVDPOLYPR O_1 Bovine viral diarrhea virus polyprotein RNA, complete cds; Putative	1	
71	Y08559	B.subtilis urease operon and downstream DNA.	0.99	LRP_CAEEL	LOW-DENSITY LIPOPROTEIN RECEPTOR- RELATED PROTEIN PRECURSOR (LRP)>PIR2:A47437 LDL-receptor-related protein - Caenorhabditis elegans>GP:CEF29D1 1_2 Caenorhabditis elegans cosmid F29D11, complete sequence; F29D11;1; Protein predicted using Genefi	1	

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	Nearest			Nearest		
	Neighbor			Neighbor		
	(BlastN vs.			(BlastX vs.		
	Genbank)			Non-		
				Redundant		
	ACCESSION	DESCRIPTION	P	Proteins) ACCESSION	DECODIDETON	P
SEQ ID	ACCESSION	DESCRIPTION	VALUE	ACCESSION	DESCRIPTION	VALUE
72	U67548	Mathanasasaus		VD60 VEAC	HYPOTHETICAL 16.3	1 1
/2	06/348	Methanococcus jannaschii from	0.99	YB60_YEAS T	KD PROTEIN IN	1
		bases 986219 to		1		
		996377 (section			DUR1,2-NGR1 INTERGENIC	
		90 of 150) of the			REGION>PIR2:S4608	
		complete				
		genome.			4 probable membrane protein YBR210w -	
		genome.			yeast (Saccharomyces	
					cerevisiae)>GP:SCYB	
					R210W 1 S; cerevisiae	
					chromosome II reading	
					frame ORF YBR210w	
73	U51645	Plasmodium	0.99	HPSVRPL 1	Sin Nombre virus (NM	0.99
13	031043	falciparum	0.55		H10) RNA L segment	0.55
		cytidine			encoding RNA	
		triphosphate			polymerase (L protein),	
		synthetase gene,			complete cds; Viral	
		complete cds.	,		RNA polymerase (L	
		complete cus.			protein);	
					Putative>GP:HPSVRP	
					LA 1 Sin Nombre	
					virus (NM R11) RNA	
					L segment encoding	
					RNA polymerase (L	
					protein), complete cds;	
	-				Vir	
74	Z49889	Caenorhabditis	0.99	MUSHDPRO	Mouse alternatively	0.021
		elegans cosmid		B_1	spliced HD protein	-
		тобн11,		_	mRNA, complete cds	
		complete			1	
		sequence.				
75	Z69374	Human DNA	0.99	NCPR_YEAS	NADPH-	0.017
		sequence from		\overline{T}	CYTOCHROME P450	
		cosmid L174G8,			REDUCTASE (EC	
		Huntington's			1.6.2.4) (CPR)	
		Disease Region,			, , ,	
		chromosome				
		4p16.3 contains a				
		pair of ESTs.				
		-				

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	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant			
SEQ	ACCESSION	DESCRIPTION	P	Proteins) ACCESSION	DESCRIPTION	P	
76	Z35847	S.cerevisiae chromosome II reading frame ORF YBL086c.	0.99	CYPA_CAEE L	PEPTIDYL-PROLYL CIS-TRANS ISOMERASE 10 (EC 5.2.1.8) (PPIASE) (ROTAMASE) (CYCLOPHILIN- 10)>GP:CELB0252_4 Caenorhabditis elegans cosmid B0252; Similar to peptidyl-prolyl cis- trans isomerase (PPIASE) (CYCLOPHILIN)>GP:	0.0044	
77	L35330	Rattus norvegicus glutathione S-transferase Yb3 subunit gene, complete cds.	0.99	CELR148_1	CEU34954_1 Caenorhabditis el Caenorhabditis elegans cosmid R148; Contains similarity to drosophila DNA-binding protein K10 (NID:g8148); coded for by C; elegans cDNA yk118e11;5; coded for by C; elegans cDNA	0.0032	
78	Y00324	Chicken vitellogenin gene 3' flanking region.	0.99	A56922	transcription factor shn - fruit fly (Drosophila melanogaster)	0.0023	
79	M32659	D.melanogaster Shab11 protein mRNA, complete cds.	0.99	OMU25146_1	Oncorhynchus mykiss recombination activating protein 2 gene, partial cds	0.0017	
80	Z69880	H.sapiens SERCA3 gene (partial).	0.99	M84D_DRO ME	MALE SPECIFIC SPERM PROTEIN MST84DD>PIR2:S257 75 testis-specific protein Mst84Dd - fruit fly (Drosophila melanogaster)>GP:DM MST84D_4 D;melanogaster Mst84Da, Mst84Db, Mst84Dc and Mst84Dd genes for put; sperm protein	0.0011	

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	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
81	M99166	Escherichia coli Trp repressor binding protein (wrbA) gene, complete cds.	0.99	MTU88962_1	Mycobacterium tuberculosis unknown protein gene, partial cds	6.50E-07
82	X99257	R.norvegicus mRNA for lamin C2.	0.99	MIU68729_1	Meloidogyne incognita cuticle preprocollagen (col-2) mRNA, complete cds; Putative	1.60E-09
83	AC002432	Human BAC clone RG317G18 from 7q31, complete sequence.	0.98	1FMDC	Foot and mouth disease virus type c-s8c1, chain C - foot and mouth disease virus type c-s8c1 expressed in hamster kidney cells	0.14
84	Z34799	Caenorhabditis elegans cosmid F34D10, complete sequence.	0.98	MMU57368_1	repeat transmembrane protein mRNA, complete cds; Notch like repeats; notch 2	0.0028
85	B15207	344E15.TV CIT978SKA1 Homo sapiens genomic clone A- 344E15.	0.98	POLG_HCVJ 6	GENOME POLYPROTEIN (CONTAINS: CAPSID PROTEIN C (CORE PROTEIN); MATRIX PROTEIN (ENVELOPE PROTEIN M); MAJOR ENVELOPE PROTEIN E; NONSTRUCTURAL PROTEINS NS1, NS2, NS4A AND NS4B; HELICASE (NS3); RNA-DIRECTED RNA POLYMERASE (EC 2.7.7.48) (NS5))>PI	0.00083

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	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant			
SEQ	ACCESSION	DESCRIPTION	P	Proteins) ACCESSION	DESCRIPTION	P	
ID	ACCESSION	DESCRIPTION	VALUE	ACCESSION	DESCRIPTION	VALUE	
86	AC002412	*** SEQUENCING IN PROGRESS *** Human Chromosome X; HTGS phase 1, 2 unordered pieces.	0.98	H	DIACYLGLYCEROL KINASE 1 (EC 2.7.1.107) (DIGLYCERIDE KINASE) (DGK 1) (DAG KINASE 1)>PIR2:S71467 diacylglycerol kinase (EC 2.7.1.107) ATDGK1- Arabidopsis thaliana>GP:ATHATD GK1_1 Arabidopsis thaliana mRNA for diacylglycerol kinase, complete c	0.00024	
87	X57010	Human COL2A1 gene for collagen II alpha 1 chain, exons E2-E15.	0.98	D80005_1	Human mRNA for KIAA0183 gene, partial cds	5.90E-10	
88	M83093	Neurospora crassa cAMP- dependent protein kinase (cot-1) gene, complete cds.	0.98	YA53_SCHP O	HYPOTHETICAL 24.2 KD PROTEIN C13A11.03 IN CHROMOSOME I>GP:SPAC13A11_3 S;pombe chromosome I cosmid c13A11; Unknown; SPAC13A11;03, unknown, len: 210	3.00E-22	
89	U96271	Helicobacter pylori heat shock protein 70 (hsp70) gene, complete cds.	0.97	SLMEN6_1	S;latifolia mRNA for Men-6 protein>GP:SLMEN6_ 1 S;latifolia mRNA for Men-6 protein	0.43	
90	U49944	Caenorhabditis elegans cosmid C39E6.	0.97	RON_HUMA N	MACROPHAGE STIMULATING PROTEIN RECEPTOR PRECURSOR (EC 2.7.1.112)>PIR2:I3818 5 protein-tyrosine kinase (EC 2.7.1.112), receptor type ron - human>GP:HSRON_1 H;sapiens RON mRNA for tyrosine kinase; Putative	0.034	

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	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant		
SEQ	ACCESSION	DESCRIPTION	P	Proteins) ACCESSION	DESCRIPTION	P
ID	Recepsion	BESCHIII IIOI	VALUE	RecEssion	DESCRIPTION	VALUE
91	Y09255	B.cereus dnal gene, partial.	0.97	CELT05C1_5	Caenorhabditis elegans cosmid T05C1; Coded for by C; elegans cDNA yk30f6;3; coded for by C; elegans cDNA yk34f10;3	0.00043
92	AC002413	*** SEQUENCING IN PROGRESS *** Human Chromosome X; HTGS phase 1, 2 unordered pieces.	0.96	CELC44E4_5	cosmid C44E4; Weak similarity to the drosophila hyperplastic disc protein (GB:L14644); coded for by C; elegans cDNA yk49h6;5; coded for by C; elegans cDNA	1
93	U41625	Caenorhabditis elegans cosmid K03A1.	0.96	HMGC_HUM AN	HIGH MOBILITY GROUP PROTEIN HMGI- C>PIR2:JC2232 high mobility group I-C phosphoprotein - human>GP:HSHMGIC G5_1 Human high- mobility group phosphoprotein isoform I-C (HMGIC) gene, exon 5>GP:HSHMGICP_1 H;sapiens mRNA for HMGI-C protein>GP:HSHMGIC	1
94	Z82202	Human DNA sequence *** SEQUENCING IN PROGRESS *** from clone 34P24; HTGS phase 1.	0.96	YTH3_CAEE L	HYPOTHETICAL 75.5 KD PROTEIN C14A4.3 IN CHROMOSOME II>GP:CEC14A4_3 Caenorhabditis elegans cosmid C14A4, complete sequence; C14A4;3; Weak similarity with a B; Flavum translocation protein (Swiss Prot accession number P38376)	0.73

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
95	AL008734	Human DNA sequence *** SEQUENCING IN PROGRESS *** from clone 324M8; HTGS phase 1.	0.96	S25299	extensin precursor (clone Tom L-4) - tomato>GP:TOMEXT ENB_1 L;esculentum extensin (class II) gene, complete cds	0.0004
96	L15388	Human G protein-coupled receptor kinase (GRK5) mRNA, complete cds.	0.96	HUMCOL7A1 X_1	Homo sapiens (clones: CW52-2, CW27-6, CW15-2, CW26-5, 11- 67) collagen type VII intergenic region and (COL7A1) gene, complete cds	4.60E-06
97	X97384	A.thaliana atran3 gene.	0.95	<none></none>	<none></none>	<none></none>
98	M62505	Human C5a anaphylatoxin receptor mRNA, complete cds.	0.95	RIPB_BRYDI	RIBOSOME- INACTIVATING PROTEIN BRYODIN (RRNA N- GLYCOSIDASE) (EC 3.2.2.22) (FRAGMENT)>PIR2: S16491 rRNA N- glycosidase (EC 3.2.2.22) bryodin - red bryony (fragment)	0.83
99	D28778	Cucumber mosaic virus RNA 1 for 1a, complete sequence.	0.95	POLS_RUBV M	STRUCTURAL POLYPROTEIN (CONTAINS: NUCLEOCAPSID PROTEIN C; MEMBRANE GLYCOPROTEINS E1 AND E2)>PIR1:GNWVR3 structural polyprotein - rubella virus (strain M33)>GP:TORUB24S _1 Rubella virus 24S subgenomic mRNA for structural proteins E1, E2 and C;	0.00037
100	AF016202	Homo sapiens immunoglobulin heavy chain CDR3 gene,	0.93	HSU79716_1	Human reelin (RELN) mRNA, complete cds	1

Table 2

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant		
				Proteins)		
SEQ ID	ACCESSION		P VALUE	ACCESSION	DESCRIPTION	P VALUE
		partial cds.				
101	Z68303	Caenorhabditis elegans cosmid ZK809, complete sequence.	0.93	HS5HT4SAR_ 1	H;sapiens mRNA for serotonin 4SA receptor (5-HT4SA-R)	0.87
102	X03049	E. coli DNA sequene 5' to origin of replication oriC.	0.93	S37594	mucin - human (fragment)	0.0019
103	M32659	D.melanogaster Shab11 protein mRNA, complete cds.	0.93	S38480	nonstructural protein - rubella virus>GP:RVM33NP_ 1 Rubella virus M33 RNA for a nonstructural protein; Nonstructural protein genes	2.30E-06
104	D88687	Human mRNA for KM-102- derived reductase-like factor, complete cds.	0.93	N	LARGE PROLINE- RICH PROTEIN BAT3 (HLA-B- ASSOCIATED TRANSCRIPT 3)>PIR2:A35098 MHC class III histocompatibility antigen HLA-B- associated transcript 3 - human>GP:HUMBAT 3A_1 Human HLA-B- associated transcript 3 (BAT3) mRNA, complete cds>GP:HUMBAT3	8.70E-07
105	D16847	Mouse mRNA for stromal cell derived protein-1, complete cds.	0.93	S52796	prpL2 protein - human (fragment)>GP:HSPRP L2_1 H;sapiens mRNA for PRPL-2 protein	3.20E-08

Table 2

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
106	D90915	Synechocystis sp. PCC6803 complete genome, 17/27, 2137259-2267259.	0.92	YEK9_YEAS T	HYPOTHETICAL 53.9 KD PROTEIN IN AFG3-SEB2 INTERGENIC REGION>PIR2:S5047 7 hypothetical protein YER019w - yeast (Saccharomyces cerevisiae)>GP:SCE95 37_20 Saccharomyces cerevisiae chromosome V cosmids 9537, 9581, 9495, 9867, and lambda clone 5898	5.90E-05
107	AJ001101	Mus musculus mRNA for gC1qBP gene.	0.92	DMU58282_1	Drosophila melanogaster Bowel (bowl) mRNA, complete cds; Transcription factor; C2H2 zinc finger protein; zinc fingers have extensive sequence similarity to Drosophila odd- skipped	3.50E-05
108	X57108	Human gene for cerebroside sulfate activator protein, exons 10- 14.	0.92	S69032	hypothetical protein YPR144c - yeast (Saccharomyces cerevisiae)>GP:YSCP9 659_17 Saccharomyces cerevisiae chromosome XVI cosmid 9659; Ypr144cp; Weak similarity near C- terminus to RNA Polymerase beta subunit (Swiss Prot; accession number P11213)	4.30E-21

Table 2

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
109	D14635	Caenorhabditis elegans DNA for EMB-5.	0.91	YM13_YEAS T	PUTATIVE ATP- DEPENDENT RNA HELICASE YMR128W>PIR2:S53 058 probable membrane protein YMR128w - yeast (Saccharomyces cerevisiae)>GP:SC955 3_4 S;cerevisiae chromosome XIII cosmid 9553; Unknown; YM9553;04, probable ATP- dependent RNA helicase, len:	0.69
110	B55500	CIT-HSP- 387J2.TFB CIT- HSP Homo sapiens genomic clone 387J2.	0.91	U97553_79	Murine herpesvirus 68 strain WUMS, complete genome; Unknown	0.00016
111	X03049	E. coli DNA sequene 5' to origin of replication oriC.	0.9	POL_MLVAV	POL POLYPROTEIN (PROTEASE (EC 3.4.23); REVERSE TRANSCRIPTASE (EC 2.7.7.49); RIBONUCLEASE H (EC 3.1.26.4))>PIR1:GNM VGV pol polyprotein - AKV murine leukemia virus	0.0019
112		Human chromosome 12p15 BAC clone CIT987SK-99D8 complete sequence.	0.89	JC5568	serine protease (EC 3.4) h1 - Serratia marcescens	1
113	X13295	Rat mRNA for alpha-2u globulin-related protein.	0.89	MNGPOLY_1	Mengo virus polyprotein genome, complete cds withe repeats	1
114	Z78415	Caenorhabditis elegans cosmid C17G1, complete sequence.	0.89	AB000121_1	Mouse mRNA for TBPIP, complete cds; TBP1 interacting protein	0.39

Table 2

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant Proteins)		
SEQ	ACCESSION	DESCRIPTION	P	ACCESSION	DESCRIPTION	P
ID			VALUE			VALUE
115	AC002308	*** SEQUENCING IN PROGRESS *** Human Chromosome 22q11 BAC Clone 1000e4; HTGS phase 1, 26 unordered pieces.	0.88	YLK2_CAEE L	HYPOTHETICAL 122.7 KD PROTEIN D1044.2 IN CHROMOSOME III>GP:CELD1044_4 Caenorhabditis elegans cosmid D1044	0.0037
116	AC002073	Human PAC clone DJ515N1 from 22q11.2- q22, complete sequence.	0.88	S28499	probable finger protein - rat>GP:RNZFP_1 R;norvegicus mRNA for putative zinc finger protein	1.10E-31
117	Z83848	Human DNA sequence *** SEQUENCING IN PROGRESS *** from clone 57A13; HTGS phase 1.	0.87	NDL_DROM E	SERINE PROTEASE NUDEL PRECURSOR (EC 3.4.21)>PIR2:A57096 nudel protein precursor - fruit fly (Drosophila melanogaster)>GP:DM U29153_1 Drosophila melanogaster nudel (ndl) mRNA, complete cds; Serine protease; Soma dependent gene required matern	1
118	U23449	Caenorhabditis elegans cosmid K06A1.	0.87	AF023268_3	Homo sapiens clk2 kinase (CLK2), propin1, cote1, glucocerebrosidase (GBA), and metaxin genes, complete cds; metaxin pseudogene and glucocerebrosidase pseudogene; and thrombospondin3 (THBS3)	0.21
119	Z68181	H.vulgaris mRNA for elongation factor EF1-alpha.	0.87	RABCY450C _1	Rabbit cytochrome P- 450 gene, clone pP- 450PBc3, 3' end	0.14

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	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
120	AC000033	Homo sapiens	0.87	VWF_CANF	VON WILLEBRAND	0.036
		chromosome 9, complete sequence.		Α	FACTOR PRECURSOR>GP:DO GVWG_1 Canis familiaris von Willebrand factor mRNA, complete cds	
121	U23449	Caenorhabditis elegans cosmid K06A1.	0.86	S48988_1	CRP-1=cystatin-related protein [rats, Wistar albino, mRNA Partial, 213 nt]; Cystatin-related protein; Method: conceptual translation supplied by author; This sequence comes from Fig;	0.64
122	Z89651	F.rubripes GSS sequence, clone 090124cD5.	0.86	CPU65981_1	Cryptosporidium parvum P-ATPase gene (CppA-E1) gene, complete cds; Putative calcium-ATPase	0.6
123	Z94055	Human DNA sequence from PAC 24M15 on chromosome 1. Contains tenascin-R (restrictin), EST.	0.86	GLTB_SYNY 3	FERREDOXIN-DEPENDENT GLUTAMATE SYNTHASE 1 (EC 1.4.7.1) (FD-GOGAT)>PIR2:S6022 8 glutamate synthase (ferredoxin) (EC 1.4.7.1) gltB - Synechocystis sp. (PCC 6803)>GP:D90902_66 Synechocystis sp; PCC6803 complete genome, 4/27, 402290- 524345; Gluta	0.03
124	Z49250	Human DNA sequence from cosmid HW2, Huntington's Disease Region, chromosome 4p16.3.	0.86	TRSCAPSID_ 1	Tobacco ringspot virus capsid protein gene, complete cds	3.00E-06

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	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
125	Z92855	Caenorhabditis elegans DNA *** SEQUENCING IN PROGRESS *** from clone Y48C3; HTGS phase 1.	0.84	AE000809_8	Methanobacterium thermoautotrophicum from bases 161632 to 172569 (section 15 of 148) of the complete genome; Aspartyl tRNA synthetase; Function Code:10;07 - Metabolism of	1
126	AC002340	*** SEQUENCING IN PROGRESS *** Arabidopsis thaliana 'TAMU' BAC 'T11J7' genomic sequence near marker 'm283'; HTGS phase 1, 2 unordered pieces.	0.83	CET01E8_3	Caenorhabditis elegans cosmid T01E8, complete sequence; T01E8;3; Similar to 1-phosphatidylinositol-4,5-bisphosphate phosphodiesterase; cDNA EST CEESG02F comes from this gene;	0.86
127		Human DNA sequence *** SEQUENCING IN PROGRESS *** from clone 206C7; HTGS phase 1.	0.83	HIVU51189_5	HIV-1 clone 93th253 from Thailand, complete genome; Tat protein	0.86
128		*** SEQUENCING IN PROGRESS *** Arabidopsis thaliana 'TAMU' BAC 'T11J7' genomic sequence near marker 'm283'; HTGS phase 1, 2 unordered pieces.	0.83	\$60257	meltrin alpha - mouse>GP:MUSMAB _1 Mouse mRNA for meltrin alpha, complete cds	0.0013

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Table 1. The sequence *** SEQUENCING IN PROGRESS *** from clone 57A13; HTGS phase 1. ARO1_PNEC PENTAFUNCTIONAL AROM POLYPEPTIDE (CONTAINS: 3-DEHYDROQUINATE SYNTHASE (EC 4.6.1.3), 3-DEHYDROQUINATE DEHYDRATASE (EC 4.2.1.10) (3-DEHYDROQUINASE) , SHIKIMATE 5-DEHYDROGENASE	P VALUE 0.0098
Genbank) SEQ ACCESSION DESCRIPTION P VALUE 129 Z83848 Human DNA sequence *** SEQUENCING IN PROGRESS *** from clone 57A 13; HTGS phase 1. SEQ phase 1. Non-Redundant Proteins) P ACCESSION DESCRIPTION ACCESSION DESCRIPTION PENTAFUNCTIONAL AROM POLYPEPTIDE (CONTAINS: 3-DEHYDROQUINATE SYNTHASE (EC 4.6.1.3), 3-DEHYDROQUINATE DEHYDROQUINATE DEHYDROQUINATE DEHYDROQUINASE), SHIKIMATE 5-DEHYDROGENASE	VALUE
Redundant Proteins) SEQ ACCESSION DESCRIPTION P ACCESSION DESCRIPTION 129 Z83848 Human DNA sequence *** SEQUENCING IN PROGRESS *** from clone 57A 13; HTGS phase 1. AROM POLYPEPTIDE (CONTAINS: 3-DEHYDROQUINATE SYNTHASE (EC 4.6.1.3), 3-DEHYDROQUINATE DEHYDROQUINATE DEHYDROQUINATE DEHYDROQUINATE DEHYDROQUINASE) , SHIKIMATE 5-DEHYDROGENASE	VALUE
SEQ ACCESSION DESCRIPTION P ACCESSION DESCRIPTION 129 Z83848 Human DNA sequence *** SEQUENCING IN PROGRESS *** from clone 57A13; HTGS phase 1. AROM POLYPEPTIDE (CONTAINS: 3-DEHYDROQUINATE SYNTHASE (EC 4.6.1.3), 3-DEHYDROQUINATE DEHYDROQUINATE DEHYDROQUINATE DEHYDROQUINATE DEHYDROQUINASE) , SHIKIMATE 5-DEHYDROGENASE	VALUE
SEQ ACCESSION DESCRIPTION P VALUE 129 Z83848 Human DNA sequence *** SEQUENCING IN PROGRESS *** from clone 57A 13; HTGS phase 1.	VALUE
ID VALUE 129 Z83848 Human DNA sequence *** SEQUENCING IN PROGRESS *** from clone 57A 13; HTGS phase 1. 129 DEHYDROQUINATE DEHYDROQUINATE DEHYDROQUINATE DEHYDROQUINATE DEHYDROQUINATE DEHYDROQUINATE DEHYDROQUINASE) , SHIKIMATE 5-DEHYDROGENASE	VALUE
Table 1. ARO1_PNEC PENTAFUNCTIONAL AROM POLYPEPTIDE	
sequence *** SEQUENCING IN PROGRESS *** from clone 57A13; HTGS phase 1. AROM POLYPEPTIDE (CONTAINS: 3- DEHYDROQUINATE SYNTHASE (EC 4.6.1.3), 3- DEHYDROQUINATE DEHYDROQUINATE DEHYDROQUINASE) , SHIKIMATE 5- DEHYDROGENASE	0.0070
SEQUENCING IN PROGRESS *** from clone 57A13; HTGS phase 1. POLYPEPTIDE (CONTAINS: 3- DEHYDROQUINATE SYNTHASE (EC 4.6.1.3), 3- DEHYDROQUINATE DEHYDROQUINATE DEHYDRATASE (EC 4.2.1.10) (3- DEHYDROQUINASE) , SHIKIMATE 5- DEHYDROGENASE	
IN PROGRESS *** from clone 57A13; HTGS phase 1. (CONTAINS: 3- DEHYDROQUINATE SYNTHASE (EC 4.6.1.3), 3- DEHYDROQUINATE DEHYDRATASE (EC 4.2.1.10) (3- DEHYDROQUINASE) , SHIKIMATE 5- DEHYDROGENASE	
*** from clone 57A13; HTGS phase 1. DEHYDROQUINATE SYNTHASE (EC 4.6.1.3), 3- DEHYDROQUINATE DEHYDROQUINATE DEHYDROQUINASE (EC 4.2.1.10) (3- DEHYDROQUINASE) , SHIKIMATE 5- DEHYDROGENASE	
57A13; HTGS phase 1. SYNTHASE (EC 4.6.1.3), 3- DEHYDROQUINATE DEHYDRATASE (EC 4.2.1.10) (3- DEHYDROQUINASE) , SHIKIMATE 5- DEHYDROGENASE	
phase 1. 4.6.1.3), 3- DEHYDROQUINATE DEHYDRATASE (EC 4.2.1.10) (3- DEHYDROQUINASE) , SHIKIMATE 5- DEHYDROGENASE	
DEHYDRATASE (EC 4.2.1.10) (3-DEHYDROQUINASE), SHIKIMATE 5-DEHYDROGENASE	ŀ
4.2.1.10) (3- DEHYDROQUINASE) , SHIKIMATE 5- DEHYDROGENASE	,
DEHYDROQUINASE) , SHIKIMATE 5- DEHYDROGENASE	
, SHIKIMATE 5- DEHYDROGENASE	
DEHYDROGENASE	
(EC 1.1.1.25),	
SHIKIMATE KINASE	
(EC 2.7.1.71), AND EPSP SYNTHASE (E	
	2.00E-08
chromosome 9 cosmid ZK84; Final	2.00L-08
duplication of the exon in repeat region;	
T cell receptor similar to long tandem	
beta locus and repeat region of	
trypsinogen gene sialidase	
families. (SP:TCNA_TRYCR,	
P23253) and	
neurofilament H	
protein; coded for by C;	
elegans	0.44
131 AC002458 Human BAC 0.78 IGF2_PIG INSULIN-LIKE GROWTH FACTOR II	0.44
clone RG098M04 GROWTH FACTOR II from 7q21-q22, PRECURSOR (IGF-	
complete FRECORSOR (IGF-	
sequence. S;scrofa mRNA IGF2	
for insulin-like-growth	
factor 2; Insulin- like-	
growth factor 2	
preproprotein	
132 Z83843 Human DNA 0.78 PAR51A_1 P;tetraurelia 51A	0.0014
sequence *** surface protein gene,	
SEQUENCING complete cds	
IN PROGRESS	
*** from clone	
368A4; HTGS	
phase 1.	

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	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
133	X03021	Human gene for granulocyte-macrophage colony stimulating factor (GM-CSF).	0.78	CEF57B1_3	Caenorhabditis elegans cosmid F57B1, complete sequence; F57B1;3; Protein predicted using Genefinder; similar to collagen	2.20E-05
134	Z74825	S.cerevisiae chromosome XV reading frame ORF YOL083w.	0.77	SYLM_SCHP O	PUTATIVE LEUCYL- TRNA SYNTHETASE, MITOCHONDRIAL PRECURSOR (EC 6.1.1.4) (LEUCINE TRNA LIGASE)>PIR2:S6248 6 hypothetical protein SPAC4G8.09 - fission yeast (Schizosaccharomyces pombe)>GP:SPAC4G8 _9 S;pombe chromosome I cosmid c4G8; Unknown; SPAC	0.96
135	Z74825	S.cerevisiae chromosome XV reading frame ORF YOL083w.	0.77	RNU59809_1	Rattus norvegicus mannose 6- phosphate/insulin-like growth factor II receptor (M6P/IGF2r) mRNA, complete cds; Also termed IGF- II/Man 6-P receptor, MPR, CI-MPR	0.01
136	U80445	Caenorhabditis elegans cosmid C50F2.	0.76	S28499	probable finger protein - rat>GP:RNZFP_1 R;norvegicus mRNA for putative zinc finger protein	1.10E-31
137	Z78545	Caenorhabditis elegans cosmid M03B6, complete sequence.	0.75	RRU73586_1	Rattus norvegicus Fanconi anemia group C mRNA, complete cds; Fanconi anemia group C protein; Similar to human FAC protein, GenBank Accession Numbers X66893 and X66894	0.023

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	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant Proteins)		
SEQ	ACCESSION	DESCRIPTION	P	ACCESSION	DESCRIPTION	P
1 D	Z97630	Human DNA	VALUE 0.74	HSMSHREC	H;sapiens mRNA for	0.036
		sequence *** SEQUENCING IN PROGRESS *** from clone 466N1; HTGS phase 1.		A_1	MSH receptor; Author- given protein sequence is in conflict with the conceptual translation	
139	AF007269	Arabidopsis thaliana BAC IG002N01.	0.71	HSU95090_1	Homo sapiens chromosome 19 cosmid F19541, complete sequence; F19541_1; Hypothetical (partial) protein similar to proline oxidase	0.16
140	AC002393	Mouse BAC284H12 Chromosome 6, complete sequence.	0.7	RNLTBP2_1	Rattus norvegicus mRNA for LTBP-2 like protein; Latent TGF- beta binding protein-2 like protein	4.40E-05
141	B15232	344G8.TV CIT978SKA1 Homo sapiens genomic clone A- 344G08.	0.67	DMSEVL2_2	Drosophila melanogaster sevenless mRNA; Put; sevenless protein (AA 1 - 2510)	0.41
142	D13748	Human mRNA for eukaryotic initiation factor 4AI.	0.66	MMU53563_1	Mus musculus Brg1 mRNA, partial cds; N- terminal region of the protein	0.00016
143	S45791	band 3-related protein=renal anion exchanger AE2 homolog [rabbits, New Zealand White, ileal epithelial cells, mRNA, 3964 nt].	0.66	POLS_RUBV R	STRUCTURAL POLYPROTEIN (CONTAINS: NUCLEOCAPSID PROTEIN C; MEMBRANE GLYCOPROTEINS E1 AND E2)>PIR1:GNWVRA structural polyprotein - rubella virus (strain RA27/3 vaccine)>GP:RUBCE2 1_1 Rubella virus RA27/3 RNA for capsid, E2 and E1 proteins; Poly	5.60E-05
144	M22462	Chicken protein p54 (ets-1)	0.66	HSHP8PROT 1	H;sapiens mRNA for HP8 protein; HP8	2.00E-06
		r- · (1)	1 00		o protein, 111 o	

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	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
		mRNA, complete cds.			peptide	
145	U27999	Human clone pDEL52A11 HLA-C region cosmid 52 genomic survey sequence.	0.65	CA18_HUMA N	1(VIII) CHAIN PRECURSOR (ENDOTHELIAL COLLAGEN)>PIR2:S 15435 collagen alpha 1(VIII) chain precursor - human>GP:HSCOL8A 1_1 Human COL8A1 mRNA for alpha 1(VIII) collagen	5.70E-06
146	M54787	N.crassa mating type a-1 protein (mt a-1) gene, exons 1-3.	0.64	I50717	vacuolar H+-ATPase A subunit - chicken (fragment)>GP:GGU22 078_1 Gallus gallus vacuolar H+-ATPase A subunit gene, partial cds	0.0046
147	AC002094	Genomic sequence from Human 17, complete sequence.	0.63	PVPVA1_1	P;vivax pva1 gene	0.1
148	U32701	Haemophilus influenzae from bases 165345 to 176101 (section 16 of 163) of the complete genome.	0.63	FABG_HAEI N	3-OXOACYL-[ACYL-CARRIER PROTEIN] REDUCTASE (EC 1.1.1.100) (3- KETOACYL-ACYL CARRIER PROTEIN REDUCTASE)>PIR2: D64051 3-oxoacyl- [acyl-carrier-protein] reductase (EC 1.1.1.100) - Haemophilus influenzae (strain Rd KW20)>GP:HIU32701 7 Haemophilus	2.00E-12
149		T.brucei serum resistance associated (SRA) mRNA for VSG- like protein.	0.61	<none></none>	- NONE>	<none></none>

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Table 2

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant		
				Proteins)		
SEQ	ACCESSION	DESCRIPTION	P	ACCESSION	DESCRIPTION	P
ID			VALUE			VALUE
150	AF027865	Mus musculus Major Histocompatibilit y Locus class II region.	0.61	A56514	chromokinesin - chicken>GP:GGU1830 9_1 Gallus gallus chromokinesin mRNA, complete cds	0.045
151	U40938	Caenorhabditis elegans cosmid D1009.	0.61	YA53_SCHP O	HYPOTHETICAL 24.2 KD PROTEIN C13A11.03 IN CHROMOSOME I>GP:SPAC13A11_3 S;pombe chromosome I cosmid c13A11; Unknown; SPAC13A11;03, unknown, len: 210	1.90E-24
152	I16670	Sequence 1 from patent US 5476781.	0.59	CELF21F8_7	Caenorhabditis elegans cosmid F21F8; Similar to eukaryotic aspartyl proteases	0.39
153	Z84468	Human DNA sequence *** SEQUENCING IN PROGRESS *** from clone 299D3; HTGS phase 1.	0.59	CLG1_YEAS T	CYCLIN-LIKE PROTEIN CLG1>PIR2:S37607 cyclin-like protein YGL215w - yeast (Saccharomyces cerevisiae)>GP:SCYG L215W_1 S;cerevisiae chromosome VII reading frame ORF YGL215w>GP:YSCC LG1CPR_1 Saccharomyces cerevisiae cyclin-like protein (CLG1) gene	0.0015
154	U00054	Caenorhabditis elegans cosmid K07E12.	0.57	<none></none>	<none></none>	<none></none>
155	M21207	Synthetic SV40 T antigen mutant pseudogene, 3' end.	0.57	1CJL2	cathepsin L (EC 3.4.22.15) mutant (F(78P)L, C25S, T110A, E176G, D178G), fragment 2 - human	0.43

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant Proteins)		
SEQ ID	ACCESSIÓN	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
156	AF020282	Dictyostelium discoideum DG2033 gene, partial cds.	0.56	AC002125_4	Homo sapiens DNA from chromosome 19- cosmid F25965, genomic sequence, complete sequence; F25965_5; Hypothetical 35;3 kDa protein similar to GTPase-activating proteins and orf3 from	0.6
157	M86352	Stigmatella aurantiaca reverse transcriptase (163 RT) gene, complete cds.	0.56	AC002398_4	Human DNA from chromosome 19- specific cosmid F25965, genomic sequence, complete sequence; F25965_3; Hypothetical 96 kDa human protein similar to alpha chimaerin; Hypothetical protein>GP:AC002398 4 Human DNA from chromosome 19- specific cosmi	4.50E-06
158	AC003101	*** SEQUENCING IN PROGRESS *** Homo sapiens chromosome 17, clone HRPC41C23; HTGS phase 1, 33 unordered pieces.	0.54	<none></none>	- <none></none>	<none></none>
159	B12117	F5L15-T7 IGF Arabidopsis thaliana genomic clone F5L15.	0.54	CEF32H2_5	Caenorhabditis elegans cosmid F32H2, complete sequence; F32H2;5; Similarity to Chicken fatty acid synthase (SW:P12276); cDNA EST yk16c2;5 comes from this gene; cDNA EST yk113h6;5 comes	1

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	Nearest			Nearest		
	Neighbor	,		Neighbor		
	(BlastN vs.			(BlastX vs.		İ
	Genbank)			Non-		
				Redundant		
				Proteins)		
SEQ	ACCESSION	DESCRIPTION	P	ACCESSION	DESCRIPTION	Р
ID			VALUE			VALUE
160	AE000664	Mus musculus TCR beta locus from bases 250554 to 501917 (section 2 of 3) of	0.54	CET01G9_6	Caenorhabditis elegans cosmid T01G9, complete sequence; T01G9;4; CDNA EST yk29b7;5 comes from	0.84
		the complete sequence.			this gene	
161	B12117	F5L15-T7 IGF Arabidopsis thaliana genomic clone F5L15.	0.54	A39718	nicotinic acetylcholine receptor alpha chain - marbled electric ray (fragments)	0.27
162	Z71261	Caenorhabditis elegans cosmid F21C3, complete sequence.	0.5	KDGE_DRO ME	EYE-SPECIFIC DIACYLGLYCEROL KINASE (EC 2.7.1.107) (RETINAL DEGENERATION A PROTEIN) (DIGLYCERIDE KINASE) (DGK)>GP:DRODAG K_1 Fruit fly mRNA for diacylglycerol kinase, complete cds	4.60E-05
163	M61831	Human S- adenosylhomocys teine hydrolase (AHCY) mRNA, complete cds.	0.49	P2C2_ARAT H	PROTEIN PHOSPHATASE 2C (EC 3.1.3.16) (PP2C)>PIR2:S55457 phosphoprotein phosphatase (EC 3.1.3.16) 2C - Arabidopsis thaliana>GP:ATHPP2 CA_1 Arabidopsis thaliana mRNA for protein phosphatase 2C	5.60E-08
164	U42608	Glycine max clathrin heavy chain mRNA, complete cds.	0.48	<none></none>	<none></none>	<none></none>

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	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
165	Z93042	Human DNA sequence *** SEQUENCING IN PROGRESS *** from clone 6B17; HTGS phase 1.	0.47	PYRD_BACS U	DIHYDROOROTATE DEHYDROGENASE (EC 1.3.3.1) (DIHYDROOROTATE OXIDASE) (DHODEHASE)>PIR1 :H39845 dihydroorotate oxidase (EC 1.3.3.1) - Bacillus subtilis>GPN:BSUB00 09_25 Bacillus subtilis complete genome (section 9 of 21): from 1598421 to 1807200;	0.002
166	AC000044	Human Chromosome 22q13 Cosmid Clone p76e10, complete sequence.	0.47	MATK_MAR PO	PROBABLE INTRON MATURASE>PIR2:A 05034 hypothetical protein 370i - liverwort (Marchantia polymorpha) chloroplast>GP:CHMP XX_21 Liverwort Marchantia polymorpha chloroplast genome DNA; ORF370i	0.0011
167	X51508	Rabbit mRNA for aminopeptidase N (partial).	0.47	S45361	LRR47 protein - fruit fly (Drosophila melanogaster)>GP:DM LRR47_1 D;melanogaster mRNA for LRR47	5.30E-07
168	Z67035	H.sapiens DNA segment containing (CA) repeat; clone AFM323yf1; single read.	0.45	JQ2246	22.5K cathepsin D inhibitor protein precursor - potato>GP:POTCATH D_1 Potato cathepsin D inhibitor protein mRNA, complete cds	0.79
169	Z93042	Human DNA sequence *** SEQUENCING IN PROGRESS *** from clone 6B17; HTGS phase 1.	0.44	SMU31768_1	Schistosoma mansoni elastase gene, 3045 bp clone, complete cds	0.0022

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Table 2

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
170	L11172	Plasmodium falciparum RNA polymerase I gene, complete cds.	0.43	HUMPKD1G0 8_1	Homo sapiens polycystic kidney disease (PKD1) gene, exons 43-46; Polycystic kidney disease 1 protein	1
171	Z95889	Human DNA sequence *** SEQUENCING IN PROGRESS *** from clone 211A9; HTGS phase 1.	0.43	A09811_1	R;norvegicus mRNA for BRL-3A binding protein; Author-given protein sequence is in conflict with the conceptual translation	0.00083
172	U32772	Haemophilus influenzae from bases 954819 to 966363 (section 87 of 163) of the complete genome.	0.43	YPT2_CAEE L	HYPOTHETICAL 21.6 KD PROTEIN F37A4.2 IN CHROMOSOME III>PIR2:S44639 F37A4.2 protein - Caenorhabditis elegans>GP:CELF37A 4_8 Caenorhabditis elegans cosmid F37A4	2.50E-28
173	Z99281	Caenorhabditis elegans cosmid Y57G11C, complete sequence.	0.42	PTU19464_1	Paramecium tetraurelia outer arm dynein beta heavy chain gene, complete cds	1
174	X04571	Human mRNA for kidney epidermal growth factor (EGF) precursor.	0.42	YEK9_YEAS T	HYPOTHETICAL 53.9 KD PROTEIN IN AFG3-SEB2 INTERGENIC REGION>PIR2:S5047 7 hypothetical protein YER019w - yeast (Saccharomyces cerevisiae)>GP:SCE95 37_20 Saccharomyces cerevisiae chromosome V cosmids 9537, 9581, 9495, 9867, and lambda clone 5898	0.99

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	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
175	U32772	Haemophilus influenzae from bases 954819 to 966363 (section 87 of 163) of the complete genome.	0.41	YPT2_CAEE L	HYPOTHETICAL 21.6 KD PROTEIN F37A4.2 IN CHROMOSOME III>PIR2:S44639 F37A4.2 protein - Caenorhabditis elegans>GP:CELF37A 4_8 Caenorhabditis elegans cosmid F37A4	7.80E-21
176	AC002053	Human Chromosome 9p22 Cosmid Clone 92f5, complete sequence.	0.4	HSU33837_1	Human glycoprotein receptor gp330 precursor, mRNA, complete cds	1
177	U88309	Caenorhabditis elegans cosmid T23B3.	0.4	DROMTTGN C_1	Drosophila melanogaster mitochondrial cytochrome c oxidase subunit I (COI) gene, 5' end, Trp-, Cys-, and Tyr-tRNA genes, NADH dehydrogenase subunit 2 (ND2) gene, 3' end	0.99
178	M34025	Human fetal Ig heavy chain variable region (clone M44) mRNA, partial cds.	0.39	DNA2_YEAS T	DNA REPLICATION HELICASE DNA2>PIR2:S48904 probable purine nucleotide-binding protein YHR164c - yeast (Saccharomyces cerevisiae)>GPN:YSC H9986_3 Saccharomyces cerevisiae chromosome VIII cosmid 9986; Dna2p: DNA replication helicase; YHR164C>GP:	1
179	AC002395	Homo sapiens; HTGS phase 1, 127 unordered pieces.	0.39	VV_MUMPE	NONSTRUCTURAL PROTEIN V (NONSTRUCTURAL PROTEIN NS1)	0.11

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
180	AC003101	*** SEQUENCING IN PROGRESS *** Homo sapiens chromosome 17, clone HRPC41C23; HTGS phase 1, 33 unordered pieces.	0.39	YLK2_CAEE L	HYPOTHETICAL 122.7 KD PROTEIN D1044.2 IN CHROMOSOME III>GP:CELD1044_4 Caenorhabditis elegans cosmid D1044	0.0001
181	Z54335	Human DNA sequence from cosmid L17A9, Huntington's Disease Region, chromosome 4p16.3. Contains VNTR and a CpG island.	0.39	HUMNFAT3 A_1	Homo sapiens NF-AT3 mRNA, complete cds	1.60E-06
182	U95743	Homo sapiens chromosome 16 BAC clone CIT987-SK65D3, complete sequence.	0.38	CEZC434_6	Caenorhabditis elegans cosmid ZC434, complete sequence; ZC434;6; CDNA EST CEESO02F comes from this gene; cDNA EST CEESS60F comes from this gene	0.18
183	AC001229	Sequence of BAC F5114 from Arabidopsis thaliana chromosome 1, complete sequence.	0.34	HSOCAM_1	H;sapiens mRNA for immunoglobulin-like domain-containing 1 protein	0.051
184	X01703	Human gene for alpha-tubulin (b alpha 1).	0.33	NTC3_MOUS E	NEUROGENIC LOCUS NOTCH 3 PROTEIN>PIR2:S453 06 notch 3 protein - mouse>GP:MMNOTC _1 M;musculus mRNA for Notch 3	0.012

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	Nearest			Nearest		
	Neighbor (BlastN vs.			Neighbor (BlastX vs.		
	Genbank)			Non-		
	Genbank)			Redundant		
				Proteins)		
SEQ	ACCESSION	DESCRIPTION	P	ACCESSION	DESCRIPTION	P
ID			VALUE			VALUE
185	Z82189	Human DNA	0.31	LG106_3	Lemna gibba	0.27
		sequence ***			negatively light-	
		SEQUENCING			regulated mRNA	
		IN PROGRESS			(Lg106); Second	
		*** from clone			longest ORF (2)	
		170A21; HTGS				
186	Z98051	phase 1. Human DNA	0.3	S34960	NADU dobridas	0.25
100	Z98031	sequence ***	0.3	334960	NADH dehydrogenase	0.25
		SEQUENCING			(ubiquinone) (EC 1.6.5.3) chain 5 -	
		IN PROGRESS			Crithidia oncopelti	
		*** from clone			mitochondrion	
		501A4; HTGS			(SGC6)>GP:MICOCN	
		phase 1.			NR 3 Crithidia	
		F			oncopelti mitochondrial	
					ND4, ND5, COI, 12S	
					ribosomal RNA genes	
					for NADH	
					dehydrogenase subunit	
					4/5, cytochrome	
					oxidase subun	
187	Z98749	Human DNA	0.3	SCKC_LEIQ	CHARYBDOTOXIN	0.12
		sequence ***		Н	(CHTX) (CHTX-	
		SEQUENCING			LQ1)>PIR2:A60963	
		IN PROGRESS			charybdotoxin 1 -	
		*** from clone			scorpion (Leiurus	
		449O17; HTGS phase 1.			quinquestriatus)>3D:2 CRD Charybdotoxin	
		pilase 1.			(nmr, 12 structures) -	
					scorpion (Leiurus	
					quinquestriatus)	
188	X96763	C.albicans CDC4	0.29	CECC4 1	Caenorhabditis elegans	1.30E-17
		gene.		3 2 3 3 .	cosmid CC4, complete	1.502 17
					sequence; CC4;a;	
					Protein predicted using	
					Genefinder;	
					preliminary prediction	j

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	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
189	U38804	Porphyra purpurea chloroplast genome, complete sequence.	0.28	HIVHCDR3C _1	Human immunodeficiency virus type 1 heavy- chain complemetarity- determining region 3 mRNA (clone 11), partial cds; Heavy- chain complementarity- determining region 3	1
					(CDR3) from HIV gp120- >GP:HIVHCDR3I_1 Human immunodeficiency virus type 1 he	
190	U20657	Human ubiquitin protease (Unph) proto-oncogene mRNA, complete cds.	0.28	HSU20657_1	Human ubiquitin protease (Unph) proto-oncogene mRNA, complete cds	5.60E-12
191	AC002037	Human Chromosome 11 Overlapping Cosmids cSRL72g7 and cSRL140b8, complete sequence.	0.27	VRP1_YEAS T	VERPROLIN>GP:SC VERPRL_1 S;cerevisiae (A364) gene for verprolin	2.00E-11
192	U58748	Caenorhabditis elegans cosmid ZK180.	0.27	EXLP_TOBA C	PISTIL-SECIFIC EXTENSIN-LIKE PROTEIN PRECURSOR (PELP)>PIR2:JQ1696 pistil extensin-like protein precursor (clone pMG15) - common tobacco>GP:NTPMG1 5_1 N;tabacum mRNA for pistil extensin like protein	4.10E-12
193	Z68013	Caenorhabditis elegans cosmid W02H3, complete sequence.	0.26	<none></none>	<none></none>	<none></none>

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant Proteins)		ł
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
194	AF017042	Dictyostelium discoideum LTR- retrotransposon Skipper, partial genomic sequence, 5' end.	0.26	SPBC31F10_1 4	II cosmid c31F10; Hypothetical protein; SPBC31F10;14c, unknown, len:1586aa, some similarity eg; to YJR140C, YJ9H_YEAST, P47171, involved in cell cycle regulation	1
195	B03174	cSRL-16e2-u cSRL flow sorted Chromosome 11 specific cosmid Homo sapiens genomic clone cSRL-16e2.	0.26	CELC30E1_7	Caenorhabditis elegans cosmid C30E1	0.38
196	X70810	E.gracilis chloroplast complete genome.	0.25	CEK10H10_8	Caenorhabditis elegans cosmid K10H10, complete sequence; K10H10;k; Protein predicted using Genefinder; preliminary prediction	0.98
197	U80024	Caenorhabditis elegans cosmid C18B10.	0.25	MMAF001794 _1	Mus musculus Treacher Collins Syndrome protein (Tcof1) mRNA, complete cds; Putative nucleolar phosphoprotein; similar to Homo sapiens Treacher Collins syndrome TCOF1 protein encoded>GP:MMAF00 1794_1 Mus musculus Treacher Collins Syndrome p	0.017

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	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant Proteins)		,
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
198	AC000591	Drosophila melanogaster (subclone 9_g3 from P1 DS01486 (D32)) DNA sequence, complete sequence.	0.25	Ī	HYPOTHETICAL 64.6 KD PROTEIN IN MRCA-PCKA INTERGENIC REGION (F574)>PIR2:E65135 hypothetical 64.6 kD protein in mrcA-pckA intergenic region - Escherichia coli (strain K- 12)>GP:ECAE000415_ 7 Escherichia coli , mrcA, yrfE, yrfF, yrfG, yrfH, yrfI	0.00068
199	AC000591	Drosophila melanogaster (subclone 9_g3 from P1 DS01486 (D32)) DNA sequence, complete sequence.	0.25	YHGE ECOL Ï	HYPOTHETICAL 64.6 KD PROTEIN IN MRCA-PCKA INTERGENIC REGION (F574)>PIR2:E65135 hypothetical 64.6 kD protein in mrcA-pckA intergenic region - Escherichia coli (strain K- 12)>GP:ECAE000415_ 7 Escherichia coli , mrcA, yrfE, yrfF, yrfG, yrfH, yrfI	0.00068
200	Z99571	Human DNA sequence *** SEQUENCING IN PROGRESS *** from clone 388N15; HTGS phase 1.	0.24	YA53_SCHP O	HYPOTHETICAL 24.2 KD PROTEIN C13A11.03 IN CHROMOSOME I>GP:SPAC13A11_3 S;pombe chromosome I cosmid c13A11; Unknown; SPAC13A11;03, unknown, len: 210	0.017
201	U00672	Human interleukin-10 receptor mRNA, complete cds.	0.24	TFDP00900	- Polypeptides entry for factor Oct-2.5	1.00E-05

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	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
202	AC003061	*** SEQUENCING IN PROGRESS *** Mouse Chromosome 6 BAC clone b245c12; HTGS phase 2, 8 ordered pieces.	0.23	CG1_HUMA N	CG1 PROTEIN>GP:HSU46 023_1 Human Xq28 mRNA, complete cds; Orf	0.00078
203	AF009420	Homo sapiens microsatellite sequence in the HNF3a gene.	0.22	PN0675	collagen alpha 1(XVIII) chain - mouse (fragment)>GP:MUSC OLLAG_1 Mouse mRNA for collagen, partial cds	0.00072
204	B18861	F20C18-Sp6 IGF Arabidopsis thaliana genomic clone F20C18.	0.22	TFDP00659	- Polypeptides entry for factor PR	0.0003
205	U00672	Human interleukin-10 receptor mRNA, complete cds.	0.22	TFDP00900	- Polypeptides entry for factor Oct-2.5	1.00E-05
206	X52105	Dictyostelium discoideum SP60 gene for spore coat protein.	0.18	<none></none>	<none></none>	<none></none>
207	L07628	Saccharopolyspor a erythraea insertion sequence IS1136, copy B, 3' end.	0.17	D88764_1	Rana catesbeiana mRNA for alpha 2 type I collagen, complete cds	0.00021
208	Z49631	S.cerevisiae chromosome X reading frame ORF YJR131w.	0.16	YSCDAL1A_ 1	Saccharomyces cerevisiae alantoinase (DAL1) gene, complete cds	1
209	Z87893	F.rubripes GSS sequence, clone 043C17aB8.	0.16	CELC27A12 8	Caenorhabditis elegans cosmid C27A12; Partial CDS; this gene begins in the neighboring clone; coded for by C; elegans cDNA yk127f1;3; coded for by C; elegans cDNA yk127f1;5	1.30E-07

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	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant Proteins)		
SEQ	ACCESSION	DESCRIPTION	P	ACCESSION	DESCRIPTION	P
ID			VALUE			VALUE
210	U92852	Rhoiptelea chiliantha maturase (matK) gene, chloroplast gene encoding chloroplast protein, complete cds.	0.15	SEU40259_5	Staphyloccous epidermidis trimethoprim resistance plasmid pSK639; Orf53	0.95
211	X62620	B.mori Abd-A gene homeobox.	0.15	ATAP22_36	Arabidopsis thaliana DNA chromosome 4, ESSA I AP2 contig fragment No; 2; Hypothetical protein; Similarity to NADH dehydrogenase, Chondrus crispus; MNOS:S59107	0.75
212	J02079	epstein-barr virus simple repeat array (ir3).	0.15	A38346	ultra-high-sulfur keratin 1 - mouse>GP:MUSSER1 _1 Mouse serine 1 ultra high sulfur protein gene, complete cds; Putative	7.50E-05
213	M35027	Vaccinia virus, complete genome.	0.14	MTF1_FUSN U	MODIFICATION METHYLASE FNUDI (EC 2.1.1.73) (CYTOSINE- SPECIFIC METHYLTRANSFER ASE FNUDI) (M.FNUDI)	0.87
214	AC003058	*** SEQUENCING IN PROGRESS *** Arabidopsis thaliana 'IGF' BAC 'F27F23' genomic sequence near marker 'CIC06E08'; HTGS phase 1, 8 unordered pieces.	0.14	HEXA_DICDI	BETA- HEXOSAMINIDASE ALPHA CHAIN PRECURSOR (EC 3.2.1.52) (N-ACETYL- BETA- GLUCOSAMINIDASE) (BETA-N- ACETYLHEXOSAMI NIDASE)>PIR2:A307 66 beta-N- acetylhexosaminidase (EC 3.2.1.52) A precursor - slime mold (Dictyostelium	0.006

Table 2

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
					discoideum)>GP:DDIN AGA_1 D;d	
215	AC001229	Sequence of BAC F5I14 from Arabidopsis thaliana chromosome 1, complete sequence.	0.13	A49281	pol protein - simian T-cell lymphotropic virus type 1, STLV-1 (isolate Bab34) (fragment)>GP:STVB ABPOLA_1 Simian T-cell leukemia virus PCR derived (pol) gene, partial sequence BAB34POL; Bases 4779-4918 EMBL ATK numbering system; BAB34POL	0.77
216	U46067	Capra hircus beta-mannosidase mRNA, complete cds.	0.12	S70663	lectin heavy chain, N-acetylgalactosamine-specific - Entamoeba histolytica (fragment)>GP:EHU33 443_1 Entamoeba histolytica GalNAc lectin heavy subunit (hgl4) gene, partial cds; N-acetylgalactosamine adherence lectin heavy subunit	0.8
217	AC000380	*** SEQUENCING IN PROGRESS *** Human Chromosome 3 pac pDJ70i11; HTGS phase 1, 2 unordered pieces.	0.12	ATFCA8_19	Arabidopsis thaliana DNA chromosome 4, ESSA I contig fragment No; 8; Unnamed protein product	0.64

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	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
218	X61207	A.brasilense hisB, H, A, F and E genes for imidazole glycerolphosphat e dehydratase, glutamine amidotransferase, phosphorybosilfo rmimino-5-amino-phosphorybosil-4-imidazolecarboxa mide isomerase, cyclase and phosphorybosil-AMP-	0.12	OCCLO2_1	O;circumcincta colost- 2 gene; Cuticular collagen	0.0074
219	AF014259	cyclohydrolase. HIV-1 Patient 1088 from Edinburgh, MA- p17 (gag) gene,	0.11	DMU88570_1	Drosophila melanogaster CREB- binding protein homolog mRNA,	1
220	AC000636	partial cds. Drosophila melanogaster (subclone 2_c11 from P1 DS07660 (D44)) DNA sequence, complete sequence.	0.11	A64829	complete cds; CBP hypothetical protein in dmsC 3' region - Escherichia coli (strain K- 12)>GP:ECAE000192_ 1 Escherichia coli , ycaD, ycaK, pflA, pflB, focA genes from bases 944908 to 955952 (section 82 of 400) of the complete genome; Hypothetical protein in dmsC	0.051
221	AC002428	Human BAC clone GS039E22 from 5q31, complete sequence.	0.11	HSNMYC2_1	Human N-myc gene exon 2; Put; N-myc protein (aa 1-263) (953 is 1st base in codon)	0.00014
222	L40949	Homo sapiens (clone AT7-5eu) opioid-receptor- like protein mRNA, 5' end.	0.11	CEUNC93_2	C;elegans unc-93 gene; Protein 2	1.20E-13

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	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
223	AL008636	Human DNA sequence *** SEQUENCING IN PROGRESS *** from clone 722E9; HTGS phase 1.	0.1	XELCOL2A1 A_1	Xenopus laevis alpha-1 collagen type II' mRNA, complete cds; Alpha-1 type II' collagen	2.60E-06
224	D86993	Human (lambda) DNA for immunoglobulin light chain.	0.1	_	Caenorhabditis elegans cosmid M02B7	1.80E-09
225	AC002539	Homo sapiens chromosome 17, clone 195o20, complete sequence.	0.098	MTCY7D11_ 17	Mycobacterium tuberculosis cosmid Y7D11; Unknown; MTCY07D11;17c; unknown, len: 186 aa, FASTA best: Q10390 Y009_MYCTU hypothetical 31;0 KD protein MTCY190;09C (299 aa) opt: 355 z- score: 316;8	0.026
226	M88165	Human interalpha-trypsin inhibitor light chain (ITI) gene, exon 1.	0.096	A54161	ryanodine-binding protein alpha form - bullfrog>GP:D21070_1 Rana catesbeiana mRNA for bullfrog skeletal muscle calcium release channel (ryanodine receptor) alpha isoform(RyR1), complete cds; Ryanodine receptor alpha isoform	1
227	Z92851	Caenorhabditis elegans DNA *** SEQUENCING IN PROGRESS *** from clone Y39G8; HTGS phase 1.	0.082	CYA7_BOVI N	ADENYLATE CYCLASE, TYPE VII (EC 4.6.1.1) (ATP PYROPHOSPHATE- LYASE) (ADENYLYL CYCLASE)	0.3

Table 2

	Nearest			Nearest		
	Neighbor			Neighbor		
	(BlastN vs.			(BlastX vs.		
	Genbank)			Non-		
				Redundant		
			,	Proteins)		
SEQ	ACCESSION	DESCRIPTION	P	ACCESSION	DESCRIPTION	P
ID			VALUE			VALUE
228	L00638	Arabidopsis	0.072	NUCM_TRY	NADH-UBIQUINONE	0.24
		thaliana ubiquitin		BB	OXIDOREDUCTASE	
		conjugating			49 KD SUBUNIT	ĺ
		enzyme exons 2-			HOMOLOG (EC	
		4.			1.6.5.3) (NADH	
					DEHYDROGENASE	
					SUBUNIT 7	
		:			HOMOLOG)>PIR2:A3	
					5693 NADH	
,					dehydrogenase (EC	
					1.6.99.3) chain 7 -	
					Trypanosoma brucei	
220	1140170	D'-+	0.071) () (() () () ()	mitochondrion (SGC6)	
229	U49169	Dictyostelium discoideum V-	0.071	MMU65594_1	Mus musculus Brca2	1
		ATPase A			mRNA, complete cds;	
		subunit (vatA)			Similar to human breast	
		mRNA, complete			cancer susceptibility gene BRCA2; Allele:	
		cds.			wild type; putative	
		cus.			tumor suppressor	
230	AF001549	Homo sapiens	0.07	PM22 HUMA		0.0078
250	Arouts49	chromosome 16	0.07	N	MYELIN PROTEIN 22	0.0078
		BAC clone		19	(PMP-	
		CIT987SK-			22)>PIR2:JN0503	
		270G1 complete		:	peripheral myelin	
		sequence.			protein 22 -	
		Soquence.			human>GP:HUMGAS	
					3X 1 Human	
					peripheral myelin	
					protein 22 (GAS3)	i
					mRNA, complete	
					cds>GP:HUMPMP22_	
					1 Human peripheral	
					myelin protein 22	
					mRNA, complete	
					cds>GP:HUMPMP22	
231	L36829	Mus musculus	0.066	<none></none>	<none></none>	<none></none>
		alphaA-crystallin-				Ī
		binding protein I				
		(AlphaA-				
		CRYBP1) gene,				
		complete cds.				
232	AC000159	***	0.058	CEZK863_1	Caenorhabditis elegans	i
		SEQUENCING		_	cosmid ZK863,	ļ
		IN PROGRESS			complete sequence;	i
		*** Human BAC			ZK863;2; Similar to	
		Clone 11q13;			collagen	
			207			

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	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
		HTGS phase 1, 10 unordered pieces.				
233	AC000159	*** SEQUENCING IN PROGRESS *** Human BAC Clone 11q13; HTGS phase 1, 10 unordered pieces.	0.058	CAC2_HAEC O	CUTICLE COLLAGEN 2C (FRAGMENT)>GP:H AECOL2C_1 H;contortus collagen 2C mRNA, 3'end	1.20E-08
234	Z23908	H. sapiens (D5S630) DNA segment containing (CA) repeat; clone AFM268zd9; single read.	0.057	VEU34999_1	Venezuelan equine encephalitis virus nonstructural and structural polyprotein genes, complete cds; Nonstructural polyprotein; Internal stop codon, readthrough occurs 5% of the time	0.0002
235	B21875	T3E8-Sp6 TAMU Arabidopsis thaliana genomic clone T3E8.	0.055	YRR2_CAEE L	HYPOTHETICAL 91.1 KD PROTEIN R144.2 IN CHROMOSOME III>GP:CELR144_7 Caenorhabditis elegans cosmid R144; Coded for by C; elegans cDNA CEESP84R; coded for by C; elegans cDNA yk23c4;5; coded for by C; elegans cDNA yk44f9;5; coded for by C; eleg	0.68
236	Z98303	Human DNA sequence *** SEQUENCING IN PROGRESS *** from clone 140H19; HTGS phase 1.	0.048	AC002330_3	Arabidopsis thaliana BAC T10P11, complete sequence; Putative zinc-finger protein; C2H2 Zn- finger signature from position 80 to 100 [CEICNKGFQRDQNL QLHRRGH]	0,99

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	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
237	D49911	Thermus thermophilus UvrA gene, complete cds.	0.044	APP1_MOUS E	AMYLOID-LIKE PROTEIN 1 PRECURSOR (APLP)>PIR2:A46362 amyloid precursor-like protein - mouse>GP:MUSAPLP _1 Mouse amyloid precursor-like protein mRNA, complete cds	8.90E-06
238	D49911	Thermus thermophilus UvrA gene, complete cds.	0.044	1_2	Mus musculus alpha- 1(XVIII) collagen (COL18A1) gene, exons 40-43, complete cds	1.60E-06
239	X78119	P.amygdalus, Batsch (Texas) prul mRNA.	0.042	CA44_HUMA N	COLLAGEN ALPHA 4(IV) CHAIN PRECURSOR>PIR1:C GHU1B collagen alpha 4(IV) chain precursor - human>GP:HSCOL4A 4_1 H;sapiens mRNA for collagen type IV alpha 4 chain; Type IV collagen alpha 4 chain	2.00E-06
240	U72877	Rana catesbeiana L-epinephrine transporter mRNA, complete cds.	0.041	Ā	HYPOTHETICAL 33.0 KD PROTEIN IN LICA 3'REGION (ORF R6)>PIR2:S42125 hypothetical protein 3 - Mycoplasma capricolum (SGC3)>GP:MYCRP MH_6 M; capricolum rpmH, rnpA and licA gene; Orf R6	0.0008
241	L39891	Homo sapiens polycystic kidney disease- associated protein (PKD1) gene, complete cds.	0.04	MUC2_HUM AN	MUCIN 2 (INTESTINAL MUCIN 2) (FRAGMENTS)	5.90E-05
242	L40390	Candida glabrata ERG3 gene, complete cds.	0.039	G01763	atrophin-1 - human>GP:HSU23851 _1 Human atrophin-1 mRNA, complete cds	9.00E-07

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	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
243	B28113	T2L16TRB TAMU Arabidopsis thaliana genomic clone T2L16.	0.038	CELZK1248_ 14	Caenorhabditis elegans cosmid ZK1248	1.60E-18
244	AC000030	00175, complete sequence.	0.033	ATFCA8_40	Arabidopsis thaliana DNA chromosome 4, ESSA I contig fragment No; 8; Glycerol-3-phosphate permease homolog; Similarity to glycerol- 3-phosphate permease - Haemophilus influenzae	0.63
245	B10738	F13G15-Sp6 IGF Arabidopsis thaliana genomic clone F13G15.	0.032	D87521_1	Mus musculus DNA- PKcs mRNA, complete cds	0.21
246	AF024503	Caenorhabditis elegans cosmid F31F4.	0.03	138344	titin - human	1
247	Z49888	Caenorhabditis elegans cosmid F47A4, complete sequence.	0.027	KSU52064_1	Kaposi's sarcoma- associated herpes-like virus ORF73 homolog gene, complete cds; Herpesvirus saimiri ORF73 homolog>GP:KSU756 98_78 Kaposi's sarcoma-associated herpesvirus long unique region, 80 putative ORF's and kaposin gene, complete cds; OR	3.40E-10
248	Z83822	Human DNA sequence from PAC 306D1 on chromosome X contains ESTs.	0.025	GRSB_BACB R	GRAMICIDIN S SYNTHETA SE II (GRAMICIDIN S BIOSYNTHESIS GRSB PROTEIN) (EC 6)	1
249	Z94161	Human DNA sequence *** SEQUENCING IN PROGRESS *** from clone N102C10; HTGS	0.025	S16323	hypothetical protein - Arabidopsis thaliana>GP:ATHB1_1 A;thaliana homeobox gene Athb-1 mRNA; Open reading frame	0.0079

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
		phase 1.				
250	AC002094	Genomic sequence from Human 17, complete sequence.	0.021	S57447	HPBRII-7 protein - human>GP:HSHPBRII 4_1 H;sapiens HPBRII- 4 mRNA>GP:HSHPBRII 7_1 H;sapiens HPBRII- 7 gene	8.20E-08
251	D79994	Human mRNA for KIAA0172 gene, partial cds.	0.021	CER10H10_1	Caenorhabditis elegans cosmid R10H10, complete sequence; R11A8;7; Protein predicted using Genefinder; Similarity to Mouse ankyrin (PIR Acc; No; S37771); cDNA EST CEESX25F comes from this gene;	7.00E-16
252	Z97635	Human DNA sequence *** SEQUENCING IN PROGRESS *** from clone 438L4; HTGS phase 1.	0.017	CELW05H7_4		0.24
253	X84996	X.laevis mRNA for selenocysteine tRNA acting factor (Staf).	0.017	JN0786	integrin beta-4 chain precursor - mouse	0.088
254	AC002543	Human BAC clone RG300C03 from 7q31.2, complete sequence.	0.013	MZLMTCYT BT_1	Mendozellus isis mitochondrial NADH dehydrogenase, and cytochrome b genes, 3' end, and transfer RNA- Ser gene; This codes for the last 43 amino acids of NADH dehydrogenase subunit 1 followed	0.044

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	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
255	U10401	Caenorhabditis elegans cosmid T20B12.	0.012	MMMHC29N 7_2	Mus musculus major histocompatibility locus class III region:butyrophilin-like protein gene, partial cds; Notch4, PBX2, RAGE, lysophatidic acid acyl transferase- alpha, palmitoyl-	0.069
256	L14593	Saccharomyces cerevisiae protein phosphatase (PTC1) gene, complete cds.	0.011	D86995_1	Human (gene 1) DNA for phosphatase 2C motif, partial cds	2.20E-14
257	U62317	Chromosome 22q13 BAC Clone CIT987SK- 384D8 complete sequence.	0.0093	P2Y8_XENL A	P2Y PURINOCEPTOR 8 (P2Y8)>GP:XLP2Y8_ 1 X;laevis mRNA for P2Y8 nucleotide receptor	0.89
258	D29655	Pig mRNA for UMP-CMP kinase, complete cds.	0.0075	AF004858_1	Mus musculus platelet activating factor receptor mRNA, partial cds; PAF-receptor	1
259	AF002992	Homo sapiens cosmid from Xq28, complete sequence.	0.0054	FBN1_BOVI N	FIBRILLIN 1 PRECURSOR>PIR2:A 55567 fibrillin I - bovine>GP:BOVXAA AA_1 Bos taurus mRNA, complete cds; Putative	0.0004
260	B20752	T19M2-T7 TAMU Arabidopsis thaliana genomic clone T19M2.	0.0043	HSVT11EP_1	Feline herpesvirus type 1 gene for immediate early protein, complete cds; Feline herpesvirus type 1 immediate early protein	3.90E-05

				TXY		
\$0000000000000000000000000000000000000	earest			Nearest		
	eighbor			Neighbor		
	BlastN vs.			(BlastX vs.		
G	enbank)			Non-		
				Redundant		
				Proteins)		
_	CCESSION	DESCRIPTION	P	ACCESSION	DESCRIPTION	P
ID			VALUE			VALUE
261	AB006699	Arabidopsis	0.0037	YHV5_YEAS	HYPOTHETICAL	0.077
		thaliana genomic		T	143.6 KD PROTEIN	
		DNA,			IN SPO16-REC104	
1		chromosome 5,			INTERGENIC	
		P1 clone: MDJ22.			REGION>PIR2:S4675	
					4 hypothetical protein	
					YHR155w - yeast	
					(Saccharomyces	
					cerevisiae)>GPN:YSC	
					H9666_15	
					Saccharomyces	
					cerevisiae chromosome	
ŀ					VIII cosmid 9666;	
					Yhr155wp; Similar to	
					Sip3p (Snf	
262	Z99128	Human DNA	0.0032	ALU1_HUM	!!!! ALU	0.0087
1		sequence ***		AN	SUBFAMILY J	
		SEQUENCING			WARNING ENTRY	
		IN PROGRESS			11111	
		*** from clone				
		422H11; HTGS				
		phase 1.				
263	B21848	T2D2-Sp6	0.0031	B31794	mdm-1 protein (clone	1.00E-05
		TAMU			c103) - mouse	
		Arabidopsis				
		thaliana genomic				
		clone T2D2.	0.005=	D 45.55		
264	L33853	Human germline	0.0027	B45550	cytochrome b homolog	0.99
		immunoglobulin			- Plasmodium yoelii	
		kappa chain				
		variable region				
		(Vk-IV subgroup)				
		for anti-B-				
		amyloid				
		autoantibodies in				
		Alzheimer's				
	2000	disease.	0.005=	110111 0 ==	TITLE OF THE STATE	
265	B36863	HS-1042-A1-	0.0027	YQK4_CAEE	HYPOTHETICAL 64.3	0.81
		F01-MR abi CIT		L	KD PROTEIN	
	ŀ	Human Genomic			C56G2.4 IN	
	ļ	Sperm Library C			CHROMOSOME	
	ļ	Homo sapiens			III>GP:CELC56G2_2	
	ļ	genomic clone			Caenorhabditis elegans	
		Plate=CT 824			cosmid C56G2	
		Col=1 Row=K.				

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	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
266	AC003041	*** SEQUENCING IN PROGRESS **** Homo sapiens chromosome 17, clone HCIT307A16; HTGS phase 1, 10 unordered pieces.	0.0024	GLB4_LAMS P	GIANT HEMOGLOBIN AIV CHAIN (FRAGMENT)>PIR2: S01810 hemoglobin AIV - tube worm (Lamellibrachia sp.) (fragment)	0.94
267	AC002315	Mouse BAC- 146N21 Chromosome X contains iduronate-2- sulfatase gene; complete sequence.	0.0022	MG42_TARM A	SRY-RELATED PROTEIN MG42 (FRAGMENT)>PIR3:I 51369 Sry-related sequence - Tarentola mauritanica (fragment)>GP:TELM G42DNA_1 Gecko MG42 gene, partial cds; Sry-related sequence	0.99
268	AF016674	Caenorhabditis elegans cosmid C03H5.	0.0015	SCYJL204C_ 1	S;cerevisiae chromosome X reading frame ORF YJL204c	1
269	AF016674	Caenorhabditis elegans cosmid C03H5.	0.0015	CEM199_3	Caenorhabditis elegans cosmid M199, complete sequence; M199;e; Protein predicted using Genefinder; preliminary prediction	0.97
270	AF016674	Caenorhabditis elegans cosmid C03H5.	0.0015	CEM199_3	Caenorhabditis elegans cosmid M199, complete sequence; M199;e; Protein predicted using Genefinder; preliminary prediction	0.97
271	Z54199	L.esculentum DNA Ailsa craig encoding 1- aminocyclopropa ne-1-carboxylic acid oxidase.	0.0015	CELF20A1_5	Caenorhabditis elegans cosmid F20A1; Coded for by C; elegans cDNA yk9g1;3; coded for by C; elegans cDNA yk9g1;5; coded for by C; elegans cDNA CEESU55F;	0.11

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	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant Proteins)			
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE	
					weak similarity to putative		
272	Z99943	Human DNA sequence *** SEQUENCING IN PROGRESS *** from clone 313L4; HTGS phase 1.	0.0014	CEK08F8_5	Caenorhabditis elegans cosmid K08F8, complete sequence; K08F8;5b	0.93	
273	S81083	beta - ADD=adducin beta subunit 63 kda isoform/membran e skeleton protein, beta - ADD=adducin beta subunit 63 kda isoform/membran e skeleton protein {alternatively spliced, exon 10 to 13 region} [human, Genomic, 1851 nt, segment 3 of 3].	0.0013	MTCY277_7	Mycobacterium tuberculosis cosmid Y277; Unknown; MTCY277;07c, unknown, len: 302	0.0001	
274	Z82174	Human DNA sequence from cosmid B20F6 on chromosome 22q11.2-qter.	0.001	FBLA_HUM AN	FIBULIN-1, ISOFORM A PRECURSOR>GP:HS FIBUA_1 H;sapiens mRNA for fibulin-1 A	0.00063	
275	Z82215	Human DNA sequence *** SEQUENCING IN PROGRESS *** from clone 68O2; HTGS phase 1.	0.00079	BFR1_SCHP O	BREFELDIN A RESISTANCE PROTEIN>PIR2:S522 39 hba2 protein - fission yeast (Schizosaccharomyces pombe)>GP:SPHBA2 GEN_1 S;pombe hba2 gene	0.15	

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	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
276	U28153	Caenorhabditis elegans UNC-76 (unc-76) gene, complete cds.	0.00071	СХ2_НЕМНА	CYTOTOXIN 2 (TOXIN 12A)	0.32
277	Z82204	Human DNA sequence from clone J362G171.	0.00054	DMU34925_2	Drosophila melanogaster DNA repair protein (mei-41) gene, complete cds, and TH1 gene, partial cds	
278	AC002530	Human BAC clone RG341D10 from 7p15-p21, complete sequence.	0.00053	CELT28F2_2	Caenorhabditis elegans cosmid T28F2; Weak similarity to HSP90	0.037
279	U91322	Human chromosome 16p13 BAC clone CIT987SK-276F8 complete sequence.	0.00051	CEW08D2_2	Caenorhabditis elegans cosmid W08D2, complete sequence; W08D2;3; Protein predicted using Genefinder>GP:CEW0 8D2_2 Caenorhabditis elegans cosmid W08D2; W08D2;3; Protein predicted using Genefinder	0.26
280	D16986	Human HepG2 partial cDNA, clone hmd2b09m5.	0.00037	POLG_PPVN A	GENOME POLYPROTEIN (CONTAINS: N- TERMINAL PROTEIN; HELPER COMPONENT PROTEINASE (EC 3.4.22) (HC-PRO); 42-50 KD PROTEIN; CYTOPLASMIC INCLUSION PROTEIN (CI); 6 KD PROTEIN; NUCLEAR INCLUSION PROTEIN; NUCLEAR INCLUSION PROTEIN A (NI- A) (EC 3.4.22) (49K PROTEINASE) (49	0.48
281	U91318	Human chromosome 16p13 BAC clone CIT987SK- 962B4 complete	0.00031	<none></none>	<none></none>	<none></none>

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	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
		sequence.				
282	M93406	Human dispersed Alu repeats and dispersed L1 repeat.	0.0003	VG8_SPV4	GENE 8 PROTEIN>PIR1:G8BP SV gene 8 protein - spiroplasma virus 4 (SGC3)	0.23
283	AC002398	Human DNA from chromosome 19- specific cosmid F25965, genomic sequence, complete sequence.	0.00021	HMCA_DRO ME	HOMEOTIC CAUDAL PROTEIN>PIR2:A263 57 homeotic protein Cad - fruit fly (Drosophila melanogaster)>GP:DR OCADA2_1 D;melanogaster caudal gene (cad) encoding a maternal and zygotic transcript, exon 2; Caudal protein>TFD:TFDP001 59 - Polypeptides en	0.021
284	AC002530	Human BAC clone RG341D10 from 7p15-p21, complete sequence.	0.0002	PL0009	complement C3d/Epstein-Barr virus receptor precursor - human	0.7
285	X01871	Yeast mitochondrial ori(o) repeat unit of petite mutant 5 (petite strain s- 10/7/2).	0.00015	RVZMTCYT BT_1	Reventazonia sp; mitochondrial NADH dehydrogenase, and cytochrome b genes, 3' end, and transfer RNA- Ser gene; This codes for the last 43 amino acids of NADH dehydrogenase subunit 1 followed	0.73
286	U89984	Acanthamoeba castellanii transformation-sensitive protein homolog mRNA, complete cds.	0.00015	ACU89984_1	Acanthamoeba castellanii transformation- sensitive protein homolog mRNA, complete cds; Similar to human transformation-	4.20E-13

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	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
					sensitive protein: SwissProt Accession Number P31948	
287	AC002365	Homo sapiens chromosome X clone U177G4, U152H5, U168D5, 174A6, U172D6, and U186B3 from Xp22, complete sequence.	0.00011	S10340	DNA-directed RNA polymerase (EC 2.7.7.6) - yeast (Kluyveromyces marxianus var. lactis)	0.00062
288	AC002390	Human DNA from overlapping chromosome 19- specific cosmids R30072 and R28588, genomic sequence, complete sequence.	9.90E-05	D86603_1	Mouse mRNA for Bach protein 1, complete cds; Bach1	1
289	AC002980	Homo sapiens; HTGS phase 1, 34 unordered pieces.	9.20E-05	TRBKPCYB_ I	Trypanosoma brucei kinetoplast apocytochrome b gene, complete cds	0.52
290	M99412	Human interleukin-8 receptor (IL8RB) gene, complete cds.	4.50E-05	S28832	microtubule-associated protein H1 (clone KS3.1) - longfin squid (fragment)	0.88
291	AC000120	Human BAC clone RG161K23 from 7q21, complete sequence.	4.00E-05	SXSCRBA_1	S;xylosus scrB and scrR genes; Sucrose repressor	0.99

Table 2

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
292	AC003037	Homo sapiens; HTGS phase 1, 66 unordered pieces.	3.40E-05	S13569	hypothetical protein 5 - Lactococcus lactis subsp. lactis insertion sequence 1076>GP:LLTLE_I Lactococcus lactis DNA for the transposon-like element on the lactose plasmid; ORF5 (AA 1 - 43)	0.018
293	Z81512	Caenorhabditis elegans cosmid F25C8, complete sequence.		MUSDBPRC_ l	Mus musculus DNA- binding protein Rc mRNA, complete cds; DNA binding protein Rc	I
294	B16681	343C3.TVB CIT978SKA1 Homo sapiens genomic clone A- 343C03.	1.10E-05	COPP_YEAS T	COATOMER BETA' SUBUNIT (BETA'- COAT PROTEIN) (BETA'- COP)>PIR2:B55123 coatomer complex beta' chain - yeast (Saccharomyces cerevisiae)>GPN:SCY GL137W_1 S;cerevisiae chromosome VII reading frame ORF YGL137w>GP:SCU11 237_1 Saccharomyces cerevisiae	0.081
295	Z16523	H. sapiens (D9S158) DNA segment containing (CA) repeat; clone AFM073yb11; single read.	1.00E-05	MMSEMF_1	M;musculus mRNA for semaphorin F; Smaphorin F	0.78
296	Z49704	S.cerevisiae chromosome XIII cosmid 8021.	5.60E-06	<none></none>	<none></none>	<none></none>
297	AC003071	Human BAC clone BK085E05 from 22q12.1-qter, complete sequence.	3.00E-06	HSRCAER_1	H;sapiens mRNA for red cell anion exchanger (EPB3, AE1, Band 3) 3' non-coding region	0.21

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	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant Proteins)		
SEQ	ACCESSION	DESCRIPTION	P	ACCESSION	DESCRIPTION	P
ID 298	U20428	Human SNC19	VALUE	HUMMUC2A	Human mucin-2 gene,	VALUE 4.40E-06
298	U2U426	mRNA sequence.	1.400-00	_1	partial cds	4.40E-00
299	U51903	Human RasGAP- related protein (IQGAP2) mRNA, complete cds.	6.60E-07	IQGA_HUMA N	RAS GTPASE-ACTIVATING-LIKE PROTEIN IQGAP1 (P195)>PIR2:A54854 Ras GTPase activating-related protein - human>GP:HUMIQG A_1 Homo sapiens ras GTPase-activating-like protein (IQGAP1) mRNA, complete cds; Amino acid feature: IQ	1.60E-14
300	AL000805	F.rubripes GSS sequence, clone 021G08aA1.	4.70E-07	MT13_MYTE D	calmodulin-binding do METALLOTHIONEIN 10-III (MT-10- III)>PIR2:S39418 metallothionein 10-III - blue mussel	2.20E-10
301	AC003016	Human BAC clone RG134C19 from 8q21, complete sequence.	4.30E-07	SPC57A10_5	S;pombe chromosome I cosmid c57A10; Unknown; SPAC57A10;05;c, unknown, len:606aa, similar to A; nidulans Q00659, sulfur metabolite repression control, (678aa), fasta scores, opt:1355,	0.00041
302	AC003089	Human BAC clone RG180F08A, complete sequence.	3.80E-07	HPBPRECK_ 1	Hepatitis B virus type 11 precore protein (pre- C region, C) gene, 5' end	0.41
303	AC002074	Human BAC clone GS056H18 from 7q31-q32, complete sequence.	2.40E-07	A47021_1	Sequence 23 from Patent WO9527787; Unnamed protein product; Author-given protein sequence is in conflict with the conceptual translation>GP:A51260 _1 Sequence 23 from Patent WO9614416; Unnamed protein product; Author-given	0.0016

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Table 2

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
			VASOL		protein sequence is i	VALGE
304	U04980	Rattus norvegicus fetal troponin T 3 (fetal TnT3) mRNA, partial cds.	2.20E-07	_	Human facioscapulohumeral muscular dystrophy (FSHD) gene region, D4Z4 tandem repeat unit; ORF	3.30E-08
305	U68704	Human chromosome 21q22.3 P1-clone 3804 subclone 4- 52.	2.00E-07	HHV6AGNM _96	Human herpesvirus-6 (HHV-6) U1102, variant A, complete virion genome; U88; Cys repeats; this loci is open in all six reading frames, part of IE-A	2.70E-05
306	U51583	Rattus norvegicus zinc finger homeodomain enhancer-binding protein-1 (Zfhep- 1) mRNA, partial cds.	8.70E-08	AF005370_67	Alcelaphine herpesvirus 1 L-DNA, complete sequence; Putative immediate early protein; ORF73; similar to H; saimiri and KSHV ORF73	6.10E-07
307	M80206	Mus domesticus poliovirus receptor homolog (MPH) mRNA, complete cds.	8.10E-08	153960	PRR2 alpha - human	1.70E-28
308	M60854	Human ribosomal protein S16 mRNA, complete cds.	5.70E-08	OLVPOL_1	Caprine arthritis encephalitis virus (isolate OVLV-N1) pol protein gene, 3' end of cds; Nt 2497-2695 from CAEV Co	0.27
309	U82828	Homo sapiens ataxia telangiectasia (ATM) gene, complete cds.	1.50E-08	C40201	artifact-warning sequence (translated ALU class C) - human	0.00044

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	Nearest			Nearest			
	Neighbor			Neighbor			
	(BlastN vs.			(BlastX vs.			
	Genbank)			Non-			
				Redundant			
~=~	+ COECGION	DESCRIPTION		Proteins)			
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE	
310	Z83836	Human DNA	1.40E-08	HSU64473 1	Human rheumatoid	0.34	
310	Z83830	sequence from	1.40E-08	пзоб44/3_1	arthritis synovium	0.34	
		PAC 111J24 on			immunoglobulin heavy		
		chromosome			chain variable region		
		22q12-qter			mRNA, partial		
		contains ESTs.			cds>GP:HSU64498_1	-	
		Comams BB 13.			Human rheumatoid		
					arthritis synovium		
					immunoglobulin heavy		
					chain variable region		
					mRNA, partial cds		
311	Z50029	Caenorhabditis	1.40E-08	MMU88984_1	Mus musculus NIK	1.70E-50	
		elegans cosmid		_	mRNA, complete cds		
		ZC504, complete					
		sequence.					
312	AC002351	Homo sapiens;	1.20E-08	D41132	collagen-related protein	0.02	
		HTGS phase 1,			4 - Hydra		
		17 unordered			magnipapillata		
		pieces.			(fragment)>PIR2:S219		
					32 mini-collagen - Hydra		
					sp.>GP:HSNCOL4_1		
					Hydra N-COL 4		
					mRNA for mini-		
					collagen; No start		
					codon		
313	B65763	CIT-HSP-	3.60E-09	S18106	type II site-specific	0.045	
		2023A12.TR			deoxyribonuclease (EC		
		CIT-HSP Homo			3.1.21.4) AbrI -		
		sapiens genomic			Azospirillum brasilense		
	7702000	clone 2023A12.	0.000.00	A D 001 (C) 12		0.7	
314	Z93021	Human DNA	2.00E-09		Chlorella vulgaris C-27	0.6	
		sequence ***		4	chloroplast DNA,		
		SEQUENCING			complete sequence;		
		IN PROGRESS *** from clone			RNA polymerase gamma subunit		
		516C23; HTGS			gamma subumi		
		phase 1.					
315	D88035	Rat mRNA for	1.50E-09	D88035 I	Rat mRNA for	1.00E-33	
	200000	glycoprotein			glycoprotein specific	2	
		specific UDP-			UDP-		
		glucuronyltransfe			glucuronyltransferase,		
		rase, complete			complete cds		
		cds.			-		
			I		L		

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Table 2

	Nearest Neighbor (BlastN vs.			Nearest Neighbor (BlastX vs. Non-		
	Genbank)			Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
316	U85193	Human nuclear factor I-B2 (NFIB2) mRNA, complete cds.	1.30E-10	VGF1_IBVB	F1 PROTEIN>PIR1:VFIH B1 F1 protein - avian infectious bronchitis virus (strain Beaudette)>GP:IBACG B_1 Avian infectious bronchitis virus pol protein, spike protein, small virion-associated protein, membrane protein, and nucleocapsid protein gen	1
317	B04719	cSRL-42G12-u cSRL flow sorted Chromosome 11 specific cosmid Homo sapiens genomic clone cSRL-42G12.	7.90E-11	JC5238	galactosylceramide-like protein, GCP - human	0.31
318	M73506	Mouse Tcp-10c (t allele) gene.	2.80E-11	A39487	T-complex protein 10a (allele 129) - mouse	4.10E-16
319	U71148	Human Xq28 cosmids U225B5 and U236A12, complete sequence.	1.20E-11	A56547	sex-peptide precursor - Drosophila suzukii	0.4
320	Z95116	Human DNA sequence *** SEQUENCING IN PROGRESS *** from clone 57G9; HTGS phase 1.	9.90E-13	ALU2_HUM AN	!!!! ALU SUBFAMILY SB WARNING ENTRY !!!!	0.0017
321	M64795	Rat MHC class I antigen gene (RT1-u haplotype), complete cds.	1.70E-14	STC_DROME	SHUTTLE CRAFT PROTEIN>GP:DMU0 9306_1 Drosophila melanogaster shuttle craft protein (stc) mRNA, complete cds; C-terminal 222 amino acids encode a novel single- stranded DNA binding domain	1.40E-13

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	Nearest Neighbor (BlastN vs. Genbank) ACCESSION DESCRIPTION P			Nearest Neighbor (BlastX vs. Non- Redundant Proteins)			
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE	
322	Y09036	H.sapiens NTRK1 gene, exon 17.	4.20E-15	_	Homo sapiens ALR mRNA, complete cds; Alternatively spliced; similarity to ALL-1 and Drosophila trithorax	1	
323	U12523	Rattus norvegicus ultraviolet B radiation- activated UV98 mRNA, partial sequence.	2.90E-15	SPBC30D10_ 4	S;pombe chromosome II cosmid c30D10; Hypothetical protein; SPBC30D10;04, unknown, len:148aa	2.40E-09	
324	Z98755	Human DNA sequence *** SEQUENCING IN PROGRESS *** from clone 76C18; HTGS phase 1.		RPON_HAL MA	DNA-DIRECTED RNA POLYMERASE SUBUNIT N (EC 2.7.7.6)>PIR2:D41715 DNA-directed RNA polymerase II chain RPB10 homolog - Haloarcula marismortui>GP:HAL HMAENOA_4 H;marismortui tRNA- Leu, HL29, HmaL13, HmaS9, OrfMMV, OrfMNA, 2- phosphoglycerate dehydr	0.019	
325	M86917	Human oxysterol- binding protein (OSBP) mRNA, complete cds.	1.60E-15	CEF14H8_2	Caenorhabditis elegans cosmid F14H8, complete sequence; F14H8;1; Similarity to Human oxysterol- binding protein (SW:OXYB_HUMAN)	2.10E-18	
326	AC001231	Genomic sequence from Human 17, complete sequence.	1.30E-15	AC002397_3	Mouse BAC284H12 Chromosome 6, complete sequence; DRPLA	0.0016	
327	AL008626	Human DNA sequence *** SEQUENCING IN PROGRESS *** from clone 1114G22; HTGS phase 1.	5.30E-16	TAU48227_1	Triticum aestivum soluble starch synthase mRNA, partial cds	5.90E-05	

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	Nearest Neighbor			Nearest Neighbor		·		
	(BlastN vs.			(BlastX vs.				
	Genbank)			Non- Redundant				
				Proteins)				
SEQ	ACCESSION	DESCRIPTION	P	ACCESSION	DESCRIPTION	P		
ID			VALUE			VALUE		
328	L04483	Human ribosomal	7.60E-17	RS21_HUMA	40S RIBOSOMAL	1.40E - 09		
		protein S21		N	PROTEIN S21>PIR2:S34108			
		(RPS21) mRNA, complete cds.			ribosomal protein S21 -			
		complete cus.			human>GP:SSZ84015			
					1 S;scrofa mRNA;			
					expressed sequence tag			
					(3'; clone c11g10); 40S			
					ribosomal protein S21;			
					Similar to human 40S			
					ribosomal protein S21>GP:HUMRPS21X			
					1 Human ribosomal			
329	AB001899	Homo sapiens	6.70E-17	LRP1 HUMA	LOW-DENSITY	1		
		PACE4 gene,		_ N	LIPOPROTEIN			
		exon 2.			RECEPTOR-			
					RELATED PROTEIN			
					1 PRECURSOR (LRP) (ALPHA-2-			
					MACROGLOBULIN			
					RECEPTOR) (A2MR)			
					(APOLIPOPROTEIN			
					E RECEPTOR)			
					(APOER)>PIR2:S0239			
					2 LDL receptor-related			
					protein precursor - human>GP:HSLDLRR			
					L_1 Human mRNA for			
					LDL-recept			
330	Z98755	Human DNA	4.40E-17	U97553_59	Murine herpesvirus 68	0.06		
		sequence ***			strain WUMS,			
		SEQUENCING			complete genome;			
		IN PROGRESS *** from clone			Ribonucleotide reductase large			
		76C18; HTGS			reductase large			
		phase 1.						
331	AF017187	Homo sapiens	3.90E-18	D84255_1	Ovophis okinavensis	0.007		
		LTR HERV-K		_	mitochondrial DNA for			
		repetitive element			NADH dehydrogenase			
		fragment			subunit 1, partial cds,			
		ltr_19_9a sequence.			Ile-tRNA, Pro-tRNA, Phe-tRNA, Gln- tRNA,			
		sequence.			Met-tRNA and control			
					region (D-loop region);			
					This cds			
					.			

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Table 2

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
332	B36252	HS-1038-A2-G01-MR.abi CIT Human Genomic Sperm Library C Homo sapiens genomic clone Plate=CT 820 Col=2 Row=M.		PGBM_MOU SE	BASEMENT MEMBRANE- SPECIFIC HEPARAN SULFATE PROTEOGLYCAN CORE PROTEIN PRECURSOR (HSPG) (PERLECAN) (PLC)>PIR2:S18252 heparan sulfate proteoglycan - mouse>GP:MUSPERP A_1 Mouse perlecan	0.00015
333	D78255	Mouse mRNA for PAP-1, complete cds.	2.70E-18	MUSPAP1_1	mRNA, complete cds Mouse mRNA for PAP-1, complete cds	3.50E-18
334	AC003046	Human Xp22 PACs RPC11- 263P4 and RPC11-164K3 complete sequence.	1.40E-18	CEC34F6_I	Caenorhabditis elegans cosmid C34F6; C34F6;1; CDNA EST yk46b12;5 comes from this gene; cDNA EST yk44c4;5 comes from this gene; cDNA EST yk46b12;3 comes from this gene	0.0015
335	AC003002	Human DNA from overlapping chromosome 19- specific cosmids R29515 and R28253, genomic sequence, complete sequence.	1.40E-18	MUSZFP0_1	Mouse mRNA for zinc finger protein, partial sequence	1.30E-19
336	Y15054	Rattus norvegicus mRNA for 70 kDa tumor specific antigen, partial.	3.40E-19	HS4U2IR2_1	Epstein-Barr virus (AG876 isolate) U2- IR2 domain encoding nuclear protein EBNA2, complete cds; Nuclear antigen 2	2.00E-06
337	Z97876	Human DNA sequence *** SEQUENCING IN PROGRESS *** from clone 295C6; HTGS	1.30E-19	AF003535_1	Homo sapiens L1 element ORF2-like protein gene, partial cds	7.00E-05

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	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant Proteins)		·
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
		phase 1.				
338	M97159	Mouse (clone pIL2) B1 dispersed repeat unit.	1.10E-19	A26882	pIL2 hypothetical protein - rat (fragment)>GP:RATT DR_1 Rat growth and transformation- dependent mRNA, 3' end; Growth and transformation dependent protein	0.2
339	U30817	Bos taurus very- long-chain acyl- CoA dehydrogenase mRNA, nuclear gene encoding mitochondrial protein, complete cds.	4.70E-20	ACDV_RAT	ACYL-COA DEHYDROGENASE, VERY-LONG-CHAIN SPECIFIC PRECURSOR (EC 1.3.99) (VLCAD)>PIR2:A548 72 acyl-CoA dehydrogenase (EC 1.3.99) very-long- chain-specific precursor - rat>GP:RATVLCAD_ 1 Rat mRNA for very- long-chain Acyl-CoA dehydrogenase, compl	8.10E-25
340	Y11535	H.sapiens mRNA for SHOXb protein.	2.80E-20	ALUI_HUM AN	!!!! ALU SUBFAMILY J WARNING ENTRY !!!!	0.00027
341	AL008730	Human DNA sequence *** SEQUENCING IN PROGRESS *** from clone 487J7; HTGS phase 1.	7.10E-21	C40201	artifact-warning sequence (translated ALU class C) - human	0.001
342	U96629	Human chromosome 8 BAC clone CIT987SK-2A8 complete sequence.	5.30E-23	ALU1_HUM AN	!!!! ALU SUBFAMILY J WARNING ENTRY !!!!	3.80E-10

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	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
343	U95743	Homo sapiens chromosome 16 BAC clone CIT987-SK65D3, complete sequence.	2.10E-24	ΑÑ	UROMODULIN PRECURSOR (TAMM-HORSFALL URINARY GLYCOPROTEIN) (THP)>PIR2:A30452 uromodulin precursor - human>GP:HUMUMO D_1 Human uromodulin (Tamm- Horsfall glycoprotein) mRNA, complete cds; Uromodulin precursor	1
344	U15972	Mus musculus homeobox (Hoxa7) gene, complete cds.	4.00E-25	S20790	extensin - almond>GP:PAEXTS_ 1 P;amygdalus mRNA for extensin	0.34
345	U15972	Mus musculus homeobox (Hoxa7) gene, complete cds.	4.00E-25	CA24_CAEE L	COLLAGEN ALPHA 2(IV) CHAIN PRECURSOR>GP:CE COLA2IV_2 C;elegans a2(IV) collagen gene; Alternatively spliced transcript	0.1
346	Z66242	H.sapiens CpG island DNA genomic Mse1 fragment, clone 84a4, reverse read cpg84a4.rt1a.	4.80E-26	CEC35A5_8	Caenorhabditis elegans cosmid C35A5, complete sequence; C35A5;8; CDNA EST yk31f6;5 comes from this gene; cDNA EST yk38h1;3 comes from this gene; cDNA EST yk38h1;5 comes from this gene;	7.70E-19
347	L25331	Rattus norvegicus lysyl hydroxylase mRNA, complete cds.	3.90E-26	K	PROCOLLAGEN- LYSINE,2- OXOGLUTARATE 5- DIOXYGENASE PRECURSOR (EC 1.14.11.4) (LYSYL HYDROXYLASE)>PI R2:A23742 procollagen-lysine 5- dioxygenase (EC 1.14.11.4) precursor - chicken>GP:CHKLYH _1 Chicken lysyl	1.10E-43

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Table 2

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
					hydroxylase mRNA, complete cds	
348	L81569	Drosophila melanogaster (subclone 2_d7 from P1 DS04260 (D68)) DNA sequence, complete sequence.	3.30E-26	CELC52B9_2	Caenorhabditis elegans cosmid C52B9; Coded for by C; elegans cDNA cm11d6; weakly similar to S; cervisiae PTM1 precursor (SP:P32857)	8.40E-29
349	U78082	Human RNA polymerase transcriptional regulation mediator (h- MED6) mRNA, complete cds.	2.30E-26	HSU78082_1	Human RNA polymerase transcriptional regulation mediator (h- MED6) mRNA, complete cds; H- Med6p	1.50E-16
350	U43381	Human Down Syndrome region of chromosome 21 DNA.	2.10E-28	HSMRNAEB_ 1	H;sapiens genomic DNA, integration site for Epstein-Barr virus; Hypothetical protein	0.18
351	D50416	Mouse mRNA for AREC3, complete cds.	2.50E-29	A29947	prostaglandin- endoperoxide synthase (EC 1.14.99.1) precursor - sheep>GP:SHPCOXA_ 1 Sheep prostaglandin endoperoxide synthetase (cyclooxygenase), complete cds; Cyclooxygenase precursor (EC 1;14;99;1)	0.81

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	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
352	U85193	Human nuclear factor I-B2 (NFIB2) mRNA, complete cds.	2.20E-29	CFU30222_1	Crithidia fasciculata fully edited ATPase subunit 6 (MURF4) mRNA, partial cds; Cryptogene	0.53
353	Z92826	Caenorhabditis elegans DNA *** SEQUENCING IN PROGRESS *** from clone C18D11; HTGS phase 1.	1.10E-30	SPAC1B3_5	S;pombe chromosome I cosmid c1B3; Hypothetical protein; SPAC1B3;05, probable transcriptional regulator, len:630aa, similar eg; to YIL038C, NOT3_YEAST, P06102, general negative regulator,	3.20E-35
354	L09604	Homo sapiens differentiation-dependent A4 protein mRNA, complete cds.	3.70E-32	PVU72769_1	Phaseolus vulgaris PvPRP-12 (Pvprp1-12) mRNA, partial cds; Similar to cell wall proline rich protein>GP:PVU72769 1 Phaseolus vulgaris PvPRP-12 (Pvprp1-12) mRNA, partial cds; Similar to cell wall proline rich protein	0.00049
355	B42455	HS-1055-B2- G03-MR.abi CIT Human Genomic Sperm Library C Homo sapiens genomic clone Plate=CT 777 Col=6 Row=N.	1.30E-32	CELT05H4_8	cosmid T05H4; Similar to the beta transducin family; coded for by C; elegans cDNA yk156e11;3; coded for by C; elegans cDNA yk14c8;3; coded for by C; elegans cDNA	6.90E-14
356	AF001905	Homo sapiens cosmids E079, B0920 and A8 from Xq25 X- linked lymphoproliferati ve disease gene candidate region, complete sequence.	1.80E-33	I38344	titin - human	1

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	Nearest Neighbor			Nearest Neighbor		
	(BlastN vs.			(BlastX vs.		
	Genbank)			Non-		
	, ,			Redundant		
				Proteins)		
SEQ	ACCESSION	DESCRIPTION	P	ACCESSION	DESCRIPTION	P
ID			VALUE			VALUE
357	E03743	DNA sequence	1.10E-34	CELC03A7_2	Caenorhabditis elegans	0.59
		including male			cosmid C03A7; Weak	
		hormone			similarity to serotonin	
		dependent gene derived from			receptors	
		hamster				
		frankorgan.				
358	U31199	Human laminin	1.20E-35	B44018	laminin B2t chain -	1.20E-14
		gamma2 chain			human>GP:HSLAMB2	
		gene (LAMC2),			TB_1 H;sapiens mRNA	
	:	exon 22 and			for laminin	
		flanking				
250	D14679	sequences. Human mRNA	2.00E-36	D49544 1	Mouse mRNA for	1.20E-23
359	D14678	for kinesin-	2.00E-30	D49344_1	KIFC1, complete cds	1.20E-23
		related protein,			Kii Ci, compicie cus	
		partial cds.				
360	AB000425	Porcine DNA for	8.20E-38	POL4_DROM	RETROVIRUS-	0.65
		endopeptidase		Е	RELATED POL	
		24.16, exon 16			POLYPROTEIN	
		and complete cds.			(PROTEASE (EC	·
					3.4.23); REVERSE TRANSCRIPTASE	
					(EC 2.7.7.49);	
					ENDONUCLEASE)	
					(TRANSPOSON	
					412)>PIR1:GNFF42	
					retrovirus-related pol	
					polyprotein - fruit fly	
					(Drosophila	
				*	melanogaster)	
					transposon 412>GP:DMRT412G	
					4	
361	U39875	Rattus norvegicus	8.80E-42	156333	apolipoprotein B - rat	0.23
		EF-hand Ca2+-			(fragment)>GP:RATA	
		binding protein			POLPB_1 Rattus	
		p22 mRNA,			norvegicus (clone	
		complete cds.			rb9E) apolipoprotein B	
					apoB mRNA, 3' end	

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Table 2

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
362	L09647	Rattus norvegicus hepatocyte nuclear factor 3a (HNF-3 beta) mRNA, complete cds.	6.60E-42	HN3B_RAT	HEPATOCYTE NUCLEAR FACTOR 3-BETA (HNF- 3B)>GP:RATHNF3B_ 1 Rattus norvegicus hepatocyte nuclear factor 3a (HNF-3 beta) mRNA, complete cds>TFD:TFDP01611 - Polypeptides entry for factor HNF-3 (beta)	8.10E-25
363	D25538	Human mRNA for KIAA0037 gene, complete cds.	4.10E-43	2 -	Caenorhabditis elegans cosmid C34D4	0.018
364	Z56764	H.sapiens CpG island DNA genomic Mse1 fragment, clone 13f7, reverse read cpg13f7.rt1a.	1.40E-43	\$75263	hypothetical protein - Synechocystis sp. (PCC 6803)>GP:D90904_29 Synechocystis sp; PCC6803 complete genome, 6/27, 630555- 781448; Hypothetical protein; ORF_ID:sll0983	0.0028
365	AC002636	*** SEQUENCING IN PROGRESS *** Drosophila melanogaster (subclone 2_g4 from P1 DS03323 (D127)) DNA sequence; HTGS phase 2.	8.40E-44	DMU95760_1	Drosophila melanogaster strawberry notch (sno) mRNA, complete cds; Notch pathway component; nuclear protein	3.40E-51
366	J05499	Rattus norvegicus L-glutamine amidohydrolase mRNA, complete cds.	8.00E-44	GLSL_RAT	GLUTAMINASE, LIVER ISOFORM PRECURSOR (EC 3.5.1.2) (GLS)>GP:RATGAH_ 1 Rattus norvegicus L- glutamine amidohydrolase mRNA, complete cds	8.00E-29

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
367	U95760	Drosophila melanogaster strawberry notch (sno) mRNA, complete cds.	5.00E-45	DMU95760_1	melanogaster strawberry notch (sno) mRNA, complete cds; Notch pathway component; nuclear protein	4.80E-45
368	L10106	Mus musculus protein tyrosine phosphate mRNA, complete cds.	4.10E-45	PTPK_HUMA N	PROTEIN-TYROSINE PHOSPHATASE KAPPA PRECURSOR (EC 3.1.3.48) (R-PTP-KAPPA)>GP:HSPTPK AP_1 H;sapiens mRNA for phosphotyrosine phosphatase kappa; Human phosphotyrosine phosphatase kappa	4.70E-16
369	D17218	Human HepG2 3' region MboI cDNA, clone hmd3g02m3.	9.40E-47	MMU53563_1		0.00012
370	U78310	Homo sapiens pescadillo mRNA, complete cds.	8.10E-48	HSU78310_1	Homo sapiens pescadillo mRNA, complete cds	1.10E-21
371	AC000399	Genomic sequence from Mouse 9, complete sequence.	7.40E-48	KIP2_YEAST	KINESIN-LIKE PROTEIN KIP2>PIR1:C42640 kinesin-related protein KIP2 - yeast (Saccharomyces cerevisiae)>GP:SCKIP 2XVI_2 S;cerevisiae PEP4 and KIP2 genes encoding PEP4 proteinase (partial) and kinesin-related protein KIP2>GP:SCLACHX VI_17 S;cerev	0.14
372	110002327	*** SEQUENCING IN PROGRESS *** Genomic sequence from Mouse 7; HTGS phase 1, 3	1.40E-48	CHKC1A205_ 1	Chicken alpha-2 type-1 collagen; amino acids - 16 to 3; Precollagen alpha-2	0.024

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# P	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
		unordered pieces.				
373	X67016	H.sapiens mRNA for amphiglycan.	9.00E-49	CED2085_2	Caenorhabditis elegans cosmid D2085, complete sequence; D2085;1; Similar to glutamine-dependent carbamoyl-phosphate synthase, aspartate carbamoyltransferase, dihydroorotase; cDNA EST cm16f3>GP:CED2085 _2 Caenorhabditis elegans cosmid D2085; D	0.14
374	L10409	Mouse fork head related protein (HNF-3beta) mRNA, complete cds.	1.50E-49	MMU04197_1	Mus musculus HNF3 beta transcription factor (HNF3b) mRNA, partial cds; Sequence of this partial cDNA begins in the first third of the conserved HNF3/forkhead DNA binding domain	1.20E-30
375	U01139	Mus musculus B6D2F1 clone 2C11B mRNA.	1.20E-49	SPBC3D5_14	S;pombe chromosome II cosmid c3D5; Unknown; SPBC3D5;14c, unknown; partial; serine rich, len:309aa, similar eg; to YNL283C, YN23_YEAST, P53832, hypothetical 52;3 kd protein, (503aa),	0.00091
376		Human DNA sequence from PAC 326L13 containing brain- 4 mRNA ESTs and polymorphic CA repeat.	9.00E-50	BSU55043_3	Bacillus subtilis plasmid pPOD2000 Rep, RapAB, RapA, ParA, ParB, and ParC genes, complete cds; ORF3	0.025

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	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
377	Z99289	Human DNA sequence *** SEQUENCING IN PROGRESS *** from clone 142L7; HTGS phase 1.	7.70E-50	A64431	hypothetical protein MJ1050 - Methanococcus jannaschii>GP:MJU67 548_2 Methanococcus jannaschii from bases 986219 to 996377 (section 90 of 150) of the complete genome; M; jannaschii predicted coding region MJ1050; Identified by GeneMark; putativ	5.60E-05
378	X98260	H.sapiens mRNA for M-phase phosphoprotein, mpp11.	6.20E-50	ZRF1_MOUS E	ZUOTIN RELATED FACTOR>GP:MMU53 208_1 Mus musculus zuotin related factor (ZRF1) mRNA, complete cds; Similar to DnaJ encoded by GenBank Accession Number L16953	3.90E-30
379	M18981	Human prolactin receptor-associated protein (PRA) gene, complete cds.	9.00E-52	S106_HUMA N	CALCYCLIN (PROLACTIN RECEPTOR ASSOCIATED PROTEIN) (PRA) (GROWTH FACTOR-INDUCIBLE PROTEIN 2A9) (S100 CALCIUM-BINDING PROTEIN A6)>PIR1:BCHUY calcyclin - human>GP:HUMCAC Y_1 Human calcyclin gene, complete cds>GP:HUMCACYA _1 Human prolactin recept	8.80E-24
380	:	Homo sapiens mRNA for KIAA0284 gene, partial cds.	1.60E-53	S33015	hypothetical protein - human herpesvirus 4	0.00088

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	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
381	U53225	Human sorting nexin 1 (SNX1) mRNA, complete cds.	1.80E-55	G02522	sorting nexin 1 - human>GP:HSU53225 _1 Human sorting nexin 1 (SNX1) mRNA, complete cds	9.20E-50
382	Z92844	Human DNA sequence from PAC 435C23 on chromosome X. Contains ESTs.	6.50E-56	D14487_1	Lentinus edodes Le;MFB1 mRNA, complete cds	1
383	D87450	Human mRNA for KIAA0261 gene, partial cds.	4.30E-56	D87450_1	Human mRNA for KIAA0261 gene, partial cds; Similar to D;melanogaster parallel sister chromatids protein	4.30E-30
384	AC002301	*** SEQUENCING IN PROGRESS *** Human chromosome +16p11.2 BAC clone CIT987SK- A-328A3; HTGS phase 2, 1 ordered pieces.	9.80E-57	\$62328	kinesin-like DNA binding protein KID - human>GP:HUMKID_ 1 Human mRNA for Kid (kinesin-like DNA binding protein), complete cds	2.60E-27
385	L29766	Homo sapiens epoxide hydrolase (EPHX) gene, complete cds.	7.30E-57	HSBCTCF4_1	Homo sapiens mRNA for hTCF-4	2.30E-05
386		Mus musculus SH3-containing protein SH3P7 mRNA, complete cds. similar to Human Drebrin.		_	Mus musculus SH3- containing protein SH3P7 mRNA, complete cds; similar to Human Drebrin; SH3- containing protein; similar to human drebrin	6.00E-43
387		Rattus norvegicus mRNA for 70 kDa tumor specific antigen, partial.	9.50E-59	RNY15054_1	Rattus norvegicus mRNA for 70 kDa tumor specific antigen, partial; 70 kD tumor- specific antigen	4.70E-45

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	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant Proteins)		
SEQ	ACCESSION	DESCRIPTION	Р	ACCESSION	DESCRIPTION	P
388	AC000406	***	7.40E-59	<none></none>	(NONE)	VALUE
		SEQUENCING IN PROGRESS *** Human Chromosome 11 overlapping pacs pDJ235k10 and pDJ239b22; HTGS phase 1, 17 unordered pieces.	7.40E-39	\NOINE>	<none></none>	<none></none>
389	L42612	Homo sapiens keratin 6 isoform K6f (KRT6F) mRNA, complete cds.	3.60E-59	KRHUEA	keratin, type II cytoskeletal - human (fragment)>GP:HSKE RA_1 Human messenger fragment encoding cytoskeletal keratin (type II); mRNA from cultured epidermal cells from human foreskin>GP:HUMKE R56K_1 Human 56k cytoskeletal type II keratin mRNA	7.60E-30
390	L29766	Homo sapiens epoxide hydrolase (EPHX) gene, complete cds.		N	EARLY GROWTH RESPONSE PROTEIN 2 (EGR-2) (KROX-20 PROTEIN) (AT591)>GP:HUMEG R2A_1 Human early growth response 2 protein (EGR2) mRNA, complete cds>TFD:TFDP00485 - Polypeptides entry for factor Egr-2	7.80E-06
391		Mus musculus homeobox protein (Hox A10) gene, 5' end of cds.	1.40E-60	PAALGYGE N_1	P;aeruginosa algY gene; Alginate lyase	0.00031
392	I29058	Sequence 3 from patent US 5576423.	4,20E-61	JC5106	stromal cell-derived factor 2 - human>GP:D50645_1 Human mRNA for SDF2, complete cds; Stroma cell-derived	1.50E-32

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	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non- Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
					factor-2	
393	129058	Sequence 3 from patent US 5576423.	4.20E-61	JC5106	stromal cell-derived factor 2 - human>GP:D50645_1 Human mRNA for SDF2, complete cds; Stroma cell-derived factor-2	1.50E-32
394	U46067	Capra hircus beta-mannosidase mRNA, complete cds.	1.90E-62	CHU46067_1	Capra hircus beta- mannosidase mRNA, complete cds	2.70E-39
395	U40747	Mus musculus formin binding protein 11 mRNA, partial cds.	6.90E-63	S64713	formin binding protein 11 - mouse (fragment)>GP:MMU4 0747_1 Mus musculus formin binding protein 11 mRNA, partial cds; FBP 11; Formin binding protein 11; tandem WWP/WW domains separated by 15 amino acid linker	3.00E-46
396	M36164	Human glyceraldehyde-3- phosphate dehydrogenase mRNA, 3' flank.	1.10E-63	BHT1UL_12	Bovine herpesvirus type 1 UL22-35 genes; UL26;5>GP:BHU3180 9_2 Bovine herpesvirus 1 maturational proteinase (UL26) gene, complete cds, and scaffold protein (UL26;5) gene, complete cds	0.003
397	Y09036	H.sapiens NTRK1 gene, exon 17.	7.30E-65		Mus musculus glucocorticoid receptor interacting protein 1 (GRIP1) mRNA, complete cds; Hormone-dependent interaction with hormone binding domains of steroid receptors;	0.0054

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	Nearest Neighbor (BlastN vs. Genbank) ACCESSION DESCRIPTION P			Nearest Neighbor (BlastX vs. Non- Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
					transactivation	
398	U17901	Rattus norvegicus phospholipase A- 2-activating protein (plap) mRNA, complete cds.	2.70E-70	JC4239	phospholipase A2- activating protein - rat	8.40E-17
399	D12646	Mouse kif4 mRNA for microtubule- based motor protein KIF4, complete cds.	1.70E-74	KIF4_MOUS E	KINESIN-LIKE PROTEIN KIF4>PIR2:A54803 microtubule-associated motor KIF4 - mouse>GP:MUSKIF4 1 Mouse kif4 mRNA for microtubule-based motor protein KIF4, complete cds; ATP- binding site: base980- 1037, motor domain: base732-1781, alpha- helical co	1.10E-44
400	AF007860	Xenopus laevis xl-Mago mRNA, complete cds.	4.60E-75	AF007862_1	Mus musculus mm- Mago mRNA, complete cds; Similar to Drosophila melanogaster Mago protein	6.50E-68
401	I45565	Sequence 15 from patent US 5637463.	2.30E-82	RNU57391_1	Rattus norvegicus FceRI gamma-chain interacting protein SH2- B (SH2-B) mRNA, complete cds; Putative FceRI gamma ITAM interacting protein; SH2 domain- containing protein B; Method: conceptual	9.90E-42

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	Nearest Neighbor (BlastN vs. Genbank) ACCESSION DESCRIPTION P			Nearest Neighbor (BlastX vs. Non- Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
402	U29156	Mus musculus eps15R mRNA, complete cds.	1.00E-85	MMU29156_1	Mus musculus eps15R mRNA, complete cds; Involved in signaling by the epidermal growth factor receptor; Method: conceptual translation supplied by author	4.90E-62
403	U70139	Mus musculus putative CCR4 protein mRNA, partial cds.	1.00E-85	MMU70139_1	Mus musculus putative CCR4 protein mRNA, partial cds; Similar to yeast transcription factor CCR4; transcriptional readthrough occurs with transcription being initiated at the IAP and continues	7.20E-66
404		Rattus norvegicus basement membrane- associated chondroitin proteoglycan Bamacan mRNA, complete cds.	7.60E-96	RNU82626_1	Rattus norvegicus basement membrane- associated chondroitin proteoglycan Bamacan mRNA, complete cds; Chondroitin sulfate proteoglycan; CSPG	8.20E-58

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Table 2

		eighbor (BlastN vs.	Genbank)	Nearest Neighbor (BlastX vs. Non-Redund	lant Proteins)
-	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
ID						
405	L09604	Homo sapiens differentiation- dependent A4 protein mRNA, complete cds.	2.00E-35	<none></none>	<none></none>	<none></none>
406	AB000516	Homo sapiens mRNA for DSIF p160, complete cds	0.41	POLG_TUMVQ	GENOME POLYPROTEIN (CONTAINS: N- TERMINAL PROTEIN; HELPER COMPONENT PROTEINASE (EC 3.4.22) (HC-PRO); 42-50 KD PROTEIN; CYTOPLASMIC INCLUSION PROTEIN (CI); 6 KD PROTEIN; VPG PROTEIN; NUCLEAR INCLUSION PROTEIN (NI-A)	2.9
407	Z94753	Human DNA sequence from PAC 465G10 on chromosome X contains Menkes Disease (ATP7A) putative Cu++- transporting P- type ATPase exons 22, 23 and STS	0.004	<none></none>	<none></none>	<none></none>
408		Homo sapiens mRNA for KIAA0551 protein, partial cds	0	MI15_CAEEL	Q23356 caenorhabditis elegans. serine/threonine- protein kinase mig- 15 (ec 2.7.1). 11/98	2.00E-51
409		Human HepG2 3' region MboI cDNA, clone hmd3g02m3	e-123	NARG_BACSU	NITRATE REDUCTASE ALPHA CHAIN (EC 1.7.99.4)	9.9
410		Bos taurus lysozyme gene (cow 2), complete cds	1.1	HAIR_MOUSE	HAIRLÉSS PROTEIN	8.00E-10

Table 2

	5	eighbor (BlastN vs.	,	Nearest Neighbor (I	BlastX vs. Non-Redund	lant Proteins)
SEQ	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
ID						
411	Z60048	H.sapiens CpG DNA, clone 187a9, reverse read cpg187a9.rt1a.	4.00E-54	HN3B_MOUSE	HEPATOCYTE NUCLEAR FACTOR 3-BETA (HNF-3B)	4.00E-21
412	Z48975	P.magnus gene for protein urPAB	0.014	YPT2_CAEEL	HYPOTHETICAL 21.6 KD PROTEIN F37A4.2 IN CHROMOSOME III	2.00E-12
413	AJ001296	Notophthalmus viridescens mRNA for cytokeratin 8	0.37	YA53_SCHPO	HYPOTHETICAL 24.2 KD PROTEIN C13A11.03 IN CHROMOSOME I	5.00E-21
414	J03831	Xenopus laevis (clone pXEC1.3) C protein mRNA, complete cds.	0.37	PDR5_YEAST	SUPPRESSOR OF TOXICITY OF SPORIDESMIN	3.3
415	AB007157	Homo sapiens gene for ribosomal protein S21, partial cds	e-142	RS21_HUMAN	40S RIBOSOMAL PROTEIN S21	0.002
416	X86340	H.sapiens C7 gene, exon 13	3.3	STC_DROME	SHUTTLE CRAFT PROTEIN	4.3
417	U12404	Human Csa-19 mRNA, complete cds.	0	R10A_PIG	60S RIBOSOMAL PROTEIN L10A (CSA-19) (FRAGMENT)	9.00E-57
418	U95102	Xenopus laevis mitotic phosphoprotein 90 mRNA, complete cds	8.00E-08	<none></none>	<none></none>	<none></none>
419	M80198	Human FKBP-12 pseudogene, clone lambda-512, 5' flank and complete cds.	5.00E-14		TRANSCRIPTIONA L REPRESSOR RCO-1	0.008
420		Homo sapiens DNA polymerase eta (POLH) mRNA, complete cds	0	<none></none>	<none></none>	<none></none>
421		Homo sapiens MAGOH mRNA, complete cds	e-131		MAGO NASHI PROTEIN	4.00E-39
422		Homo sapiens clone 23832 mRNA sequence	0.12	<none></none>	<none></none>	<none></none>

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Table 2

		ighbor (BlastN vs.	Genbank)		BlastX vs. Non-Redund	ant Proteins)
SEQ	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
ID						
423	U95098	Xenopus laevis mitotic phosphoprotein 44 mRNA, partial cds	6.00E-05	<none></none>	<none></none>	<none></none>
424	U95094	Xenopus laevis XL-INCENP (XL-INCENP) mRNA, complete cds	7.00E-07	<none></none>	<none></none>	<none></none>
425	D43952	Mouse gene for reticulocalbin, exon1 and promoter region	0.36	<none></none>	<none></none>	<none></none>
426	X68553	C.elegans repetitive DNA sequence	0.4	TCB1_RABIT	T-CELL RECEPTOR BETA CHAIN PRECURSOR (ANA 11)	0.11
427	M83314	Tomato phenylalanine ammonia lyase (pal) gene, complete cds and promoter region.	3.3	SMB2_HUMAN	DNA-BINDING PROTEIN SMUBP-2 (GLIAL FACTOR-1) (GF-1)	0.65
428		Homo sapiens clone 24686 mRNA sequence	5.00E-23	<none></none>	<none></none>	<none></none>
429	<none></none>	<none></none>	<none></none>	IQGA_HUMAN	RAS GTPASE- ACTIVATING- LIKE PROTEIN IQGAP1 (P195)	2.00E-06
430		Mus musculus DNA cytosine-5 methyltransferase 3B2 (Dnmt3b) mRNA, alternatively spliced, complete cds	5.00E-04	LOX1_LENCU	LIPOXYGENASE (EC 1.13.11.12)	9.9
431		Homo sapiens chromosome- associated polypeptide	0	YJH4_YEAST	HYPOTHETICAL 141.3 KD PROTEIN IN SCP160-MRPL8 INTERGENIC REGION	4.00E-16
432		ross river virus 26s subgenomic rna and junction region.	0.12	CUL2_HUMAN	CULLIN HOMOLOG 2 (CUL-2)	7.4

Table 2

	3	ighbor (BlastN vs.	Genbank)	Nearest Neighbor (BlastX vs. Non-Redundant Proteins)			
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE	
433		Homo sapiens properdin (PFC) gene, complete cds	0.005	UL88_HCMVA	PROTEIN UL88	5.8	
434	Z70705	H.sapiens mRNA (fetal brain cDNA com5)	2.00E-05	PH87_YEAST	INORGANIC PHOSPHATE TRANSPORTER PHO87	1.5	
435	U29156	Mus musculus eps15R mRNA, complete cds.	e-125	EP15_HUMAN	EPIDERMAL GROWTH FACTOR RECEPTOR SUBSTRATE SUBSTRATE 15 (PROTEIN EPS15) (AF-1P PROTEIN)	1.00E-13	
436	AE000750	Aquifex aeolicus section 82 of 109 of the complete genome	0.37	<none></none>	<none></none>	<none></none>	
437		Dictyostelium discoideum V- ATPase A subunit (vatA) mRNA, complete cds	0.12	VCAP_HSV6U	MAJOR CAPSID PROTEIN (MCP)	5.6	
438		Homo sapiens uncoupling protein 3 (UCP3) gene, exon 1 and partial exon 2	0.13	WEE1_SCHPO	MITOSIS INHIBITOR PROTEIN KINASE WEE1 (EC 2.7.1)	3.7	
439		Porcine DNA for endopeptidase 24.16, exon 16 and complete cds	4.00E-32	<none></none>	<none></none>	<none></none>	
440		Mus musculus 11- zinc-finger transcription factor	0.04	<none></none>	<none></none>	<none></none>	
441		Homo sapiens ubiquitin conjugating enzyme G2	e-110	<none></none>	<none></none>	<none></none>	
442		Homo sapiens clone HEB8 Cri- du-chat region mRNA	2.00E-14	LMG1_HUMAN	LAMININ GAMMA-1 CHAIN PRECURSOR (LAMININ B2 CHAIN)	8.1	

Table 2

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non-Redundant Proteins)			
SEQ	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE	
ID				!			
443	AF024578	Homo sapiens	1.1	<none></none>	<none></none>	<none></none>	
		type-1 protein					
		phosphatase skeletal muscle					
		glycogen					
		targeting subunit					
	:	(PPP1R3) gene,					
		exon 4, and					
	1/2/1/26	complete cds		D 1 0771	NOVE		
444	M24486	Human prolyl 4- hydroxylase alpha	0	DACHA	<none></none>	4.00E-58	
		subunit mRNA,					
		complete cds,					
		clone PA-11.					
445	X96400	P.tetraurelia	0.37	<none></none>	<none></none>	<none></none>	
		alpha-51D gene					
446	<none></none>	<none></none>	<none></none>	<none></none>	<none></none>	<none></none>	
447	X84996	X.laevis mRNA	0.12	POL_MLVRD	POL	2.00E-08	
		for selenocysteine tRNA acting			POLYPROTEIN		
		factor (Staf)			(PROTEASE (EC 3.4.23); REVERSE		
		(====)			TRANSCRIPTASE		
					(EC 2.7.7.49);		
					RIBONUCLEASE H		
448	AF019980	Dictyostelium	3.4	HMDL BRAFL	(EC 3.1.26.4)) HOMEOBOX	0.23	
110	111 017700	discoideum ZipA	J.4	THUDL_BKATL	PROTEIN DLL	0.23	
		(zipA) gene,			HOMOLOG		
	*****	partial cds					
449	X78424	D.carota (Queen Anne's Lace)	0.38	<none></none>	<none></none>	<none></none>	
	i	Inv*Dc2 gene,					
		3432bp					
450	<none></none>	<none></none>	<none></none>	<none></none>	<none></none>	<none></none>	
451	X89886	P.patens mRNA	1.1	CKR6_HUMAN	C-C CHEMOKINE	9.9	
		for 5- aminolevulinate			RECEPTOR TYPE 6		
		dehydratase			(C-C CKR-6) (CCR6)		
452	U67471	Methanococcus	0.12	YR72 ECOLI	HYPOTHETICAL	5.8	
		jannaschii section		-	53.2 KD PROTEIN		
		13 of 150 of the			(ORF2) (RETRON		
		complete genome			EC67)		
453	AF060246		1.00E-62	YOJ8_CAEEL	HYPOTHETICAL	1.7	
	:				1		
		mRNA, H3a-a					
l		allele, complete					
		cds		· · · · · · · · · · · · · · · · · · ·			
453		Mus musculus strain C57BL/6 zinc finger protein 106 (Zfp106) mRNA, H3a-a allele, complete	1.00E-62	YOJ8_CAEEL	'	1.7	

Table 2

		ighbor (BlastN vs.	,		BlastX vs. Non-Redund	
`	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
ID						
454	U70667	Human Fas-ligand associated factor 1 mRNA, partial cds		YKB2_YEAST	HYPOTHETICAL 69.1 KD PROTEIN IN PUT3-CCEI INTERGENIC REGION	3.00E-09
455	M95858	Bos taurus recoverin mRNA, complete cds.	0.35	GIDA_MYCGE	GLUCOSE INHIBITED DIVISION PROTEIN A	1.4
456	U67594	Methanococcus jannaschii section 136 of 150 of the complete genome	0.36	<none></none>	<none></none>	<none></none>
457		Human hnRNP core protein A1	3.00E-31	<none></none>	<none></none>	<none></none>
458		H.sapiens CpG DNA, clone 47c5, reverse read cpg47c5.rt1a.	1.3	<nöne></nöne>	<none></none>	<none></none>
459		C.jacchus intron 4 of visual pigment gene	5.00E-15	<none></none>	<none></none>	<none></none>
460		Maize stripe virus RNA 3 nonstructural protein	0.33	DSC2_MOUSE	DESMOCOLLIN 2A/2B PRECURSOR (EPITHELIAL TYPE 2 DESMOCOLLIN)	6.5
461		Yeast TEF1 gene for elongation factor EF-1 alpha	1.1	PPOL_DROME	POLY (ADP- RIBOSE) POLYMERASE (EC 2.4.2.30) (PARP)	3.5
462		S.typhimurium glutamate 1- semialdehyde aminotransferase (hemL) gene, complete cds.	1.1	EPB4_MOUSE	EPHRIN TYPE-B RECEPTOR 4 PRECURSOR (EC 2.7.1.112) KINASE 2) (TYROSINE KINASE MYK- 1)	2.5
463		Rabbit mRNA for aminopeptidase N (partial)	0.36		ACETYLCHOLINE RECEPTOR PROTEIN, GAMMA CHAIN PRECURSOR	1.5
464]]]	Mus musculus protein tyrosine phosphate mRNA, complete cds.	2.00E-58		GENE 13 PROTEIN (GP13)	2.5

Table 2

		ighbor (BlastN vs.		Nearest Neighbor (BlastX vs. Non-Redundant Proteins)			
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE	
) (55005						
465	M77235	Human cardiac tetrodotoxin-insensitive voltage-dependent sodium channel alpha subunit (HH1) mRNA, complete cds.		ZPBOC1	<none></none>	6.9	
466	M58330	C.maltosa autonomously replicating sequence.	0.004	EPB4_MOUSE	EPHRIN TYPE-B RECEPTOR 4 PRECURSOR (EC 2.7.1.112) KINASE 2) (TYROSINE KINASE MYK- 1)	2.4	
467		Rabbit mRNA for aminopeptidase N (partial)	0.35	ACHG_XENLA	ACETYLCHOLINE RECEPTOR PROTEIN, GAMMA CHAIN PRECURSOR	2.4	
468		Mus musculus protein tyrosine phosphate mRNA, complete cds.	7.00E-59	VGLI_PRVRI	GLYCOPROTEIN GP63 PRECURSOR	4.3	
469		Azotobacter vinelandii GTPase (ftsA) gene, partial cds, and ATP binding protein (ftsZ) gene, complete cds	1.1	TRUA_BACSP	Q45557 bacillus sp. (strain ksm-64). trna pseudouridine synthase a (ec 4.2.1.70) (pseudouridylate synthase i) (pseudouridine synthase i) (uracil hydrolyase). 11/98	0.001	
470	1	Mus musculus 11- zinc-finger transcription factor	0.041	<none></none>	<none></none>	<none></none>	
471		Human platelet glycoprotein IIIa, exon 14.	3.6	<none></none>	<none></none>	<none></none>	

Table 2

		eighbor (BlastN vs.	Genbank)	Nearest Neighbor (BlastX vs. Non-Redund	lant Proteins)
SEQ	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
ID						
472	U82691	Phrynocephalus raddei CAS 179770 NADH dehydrogenase subunit 1 (ND1), partial cds, tRNA-Gln, tRNA-Ile and tRNA-Met, NADH dehydrogenase subunit 2 tRNA-Cys and tRNA-Tyr and c		<none></none>	<none></none>	<none></none>
473	D85430	Mouse Murrl mRNA, exon	0.12	EPA5_CHICK	EPHRIN TYPE-A RECEPTOR 5 PRECURSOR (EC 2.7.1.112)	2.5
474	U20661	Dictyostelium discoideum unknown internal repeat protein gene, complete cds, and unknown orf1, orf2 and orf3 genes, partial cds	0.36	YHL1_EBV	HYPOTHETICAL BHLF1 PROTEIN	4.00E-04
475	X56537	Human novel homeobox mRNA for a DNA binding protein	0.04	FA5_HUMAN	COAGULATION FACTOR V PRECURSOR (ACTIVATED PROTEIN C COFACTOR)	9.5
476	U32843	Haemophilus influenzae Rd section 158 of 163 of the complete genome	5	<none></none>	<none></none>	<none></none>
477	U67554	Methanococcus jannaschii section 96 of 150 of the complete genome	0.36	<none></none>	<none></none>	<none></none>
478	AB004244	Narke japonica mRNA for Nj- synaphin 1b, complete cds	1.1	NIA1_ORYSA	NITRATE REDUCTASE 1 (EC 1.6.6.1) (NR1)	1.00E-07
479	AF075079	Homo sapiens full length insert cDNA YQ80A08	1.00E-12	<none></none>	<none></none>	<none></none>

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Table 2

	Nearest Ne	eighbor (BlastN vs.	Genbank)	Nearest Neighbor (I	BlastX vs. Non-Redund	lant Proteins)
SEQ	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
ID						
480	AE000723	Aquifex aeolicus section 55 of 109 of the complete genome	1	YKK0_YEAST	HYPOTHETICAL 67.5 KD PROTEIN IN APE1/LAP4- CWP1 INTERGENIC REGION	9.1
481	X73902	H.sapiens mRNA for nicein B2 chain	0	LMG2_HUMAN	LAMININ GAMMA-2 CHAIN PRECURSOR	3.00E-93
482	U95094	Xenopus laevis XL-INCENP (XL-INCENP) mRNA, complete cds	3.00E-10	P53_CRIGR	CELLULAR TUMOR ANTIGEN P53	5.7
483	AL010240	Plasmodium falciparum DNA *** SEQUENCING IN PROGRESS *** from contig 4-64, complete sequence	1.2	<none></none>	<none></none>	<none></none>
484	U49919	Arabidopsis thaliana lupeol synthase mRNA, complete cds	0.54	YA53_SCHPO	HYPOTHETICAL 24.2 KD PROTEIN C13A11.03 IN CHROMOSOME I	6.00E-10
485	AF077618	Homo sapiens p73 gene, exon 3	0.39	MYOD_MOUSE	MYOBLAST DETERMINATION PROTEIN I	2.1
486	AF054994	Homo sapiens clone 23832 mRNA sequence	0.13	<none></none>	<none></none>	<none></none>
487	U95102	Xenopus laevis mitotic phosphoprotein 90 mRNA, complete cds	3.00E-10	<none></none>	<none></none>	<none></none>
488		Mus musculus DNA cytosine-5 methyltransferase 3B2 (Dnmt3b) mRNA, alternatively spliced, complete cds	5.00E-04	ACE2_YEAST	METALLÖTHIONE IN EXPRESSION ACTIVATOR	1.5
489		Xenopus laevis mitotic phosphoprotein 90 mRNA, complete cds	3.00E-07	RINI_PIG	RIBONUCLEASE INHIBITOR	0.19

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Table 2

		eighbor (BlastN vs.	,		BlastX vs. Non-Redunc	lant Proteins)
SEQ	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
ID						
490	L77886	Human protein tyrosine phosphatase mRNA, complete cds	1.00E-21	VS48_TBRVS	SATELLITE RNA 48 KD PROTEIN	1.6
491	U95098	Xenopus laevis mitotic phosphoprotein 44 mRNA, partial cds	5.00E-04	CRP3_LIMPO	C-REACTIVE PROTEIN 3.3 PRECURSOR	3.5
492	U95094	Xenopus laevis XL-INCENP (XL-INCENP) mRNA, complete cds	8.00E-08	EPA5_CHICK	EPHRIN TYPE-A RECEPTOR 5 PRECURSOR (EC 2.7.1.112)	2.7
493	U95094	Xenopus laevis XL-INCENP (XL-INCENP) mRNA, complete cds	3.00E-09	<none></none>	<none></none>	<none></none>
494	U28153	Caenorhabditis elegans UNC-76 (unc-76) gene, complete cds.	0.37	<none></none>	<none></none>	<none></none>
495	U95094	Xenopus laevis XL-INCENP (XL-INCENP) mRNA, complete cds	0.37	NCPR_YEAST	NADPH- CYTOCHROME P450 REDUCTASE (EC 1.6.2.4) (CPR)	7.00E-05
496	U95102	Xenopus laevis mitotic phosphoprotein 90 mRNA, complete cds	0.013	YMB3_CAEEL	PROBABLE INTEGRIN ALPHA CHAIN F54G8.3 PRECURSOR	3.3
497	U95102	Xenopus laevis mitotic phosphoprotein 90 mRNA, complete cds	7.00E-07	<none></none>	<none></none>	<none></none>
498	U95094	Xenopus laevis XL-INCENP (XL-INCENP) mRNA, complete cds	1.00E-10	<none></none>	<none></none>	<none></none>
	U95102	Xenopus laevis mitotic phosphoprotein 90 mRNA, complete cds	2.00E-07	VGLY_LYCVW	GLYCOPROTEIN POLYPROTEIN PRECURSOR (CONTAINS: GLYCOPROTEINS G1 AND G2)	3.2

Table 2

		eighbor (BlastN vs.	Genbank)	Nearest Neighbor (E	BlastX vs. Non-Redund	lant Proteins)
SEQ	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
ID						
500	U95098	Xenopus laevis mitotic phosphoprotein 44 mRNA, partial cds	8.00E-06	HR78_DROME	NUCLEAR HORMONE RECEPTOR HR78 (DHR78) (NUCLEAR RECEPTOR XR78E/F)	2.5
501	U9 510 2	Xenopus laevis mitotic phosphoprotein 90 mRNA, complete cds	9.00E-10	MYSH_BOVIN	MYOSIN I HEAVY CHAIN-LIKE PROTEIN (MIHC) (BRUSH BORDER MYOSIN I) (BBMI)	4.00E-04
502	U95094	Xenopus laevis XL-INCENP (XL-INCENP) mRNA, complete cds	2.00E-04	BAL_HUMAN	BILE-SALT- ACTIVATED LIPASE PRECURSOR (EC 3.1.1.3) (EC 3.1.1.13) (BAL) (BILE-SALT- STIMULATED LIPASE) (BSSL) ESTERASE) (PANCREATIC LYSOPHOSPHOLIP ASE)	2.6
503	AF080399	Drosophila melanogaster mitotic checkpoint control protein kinase BUB1 (Bub1) mRNA, complete cds	1.1	NAT1_YEAST	N-TERMINAL ACETYLTRANSFE RASE 1 (EC 2.3.1.88)	2.00E-23
504	U59706	Gallus gallus alternatively spliced AMPA glutamate receptor, isoform GluR2 flop, (GluR2) mRNA, partial cds.	0.014	<none></none>	<none></none>	<none></none>
505		Xenopus laevis XL-INCENP (XL-INCENP) mRNA, complete cds	2.00E-05	<none></none>	<nöne></nöne>	<none></none>
506		Xenopus laevis mitotic phosphoprotein 44 mRNA, partial cds	2.00E-04	<none></none>	<none></none>	<none></none>

Table 2

	Nearest Ne	eighbor (BlastN vs.	Genbank)	Nearest Neighbor (1	BlastX vs. Non-Redunc	lant Proteins)
SEQ	ACCESSION		P VALUE	ACCESSION	DESCRIPTION	P VALUE
ID						TILLED
507	AF100661	Caenorhabditis elegans cosmid H20E11	0.38	<none></none>	<none></none>	<none></none>
508	U95102	Xenopus laevis mitotic phosphoprotein 90 mRNA, complete cds	3.00E-11	CAIA_HUMAN	COLLAGEN ALPHA 1(X) CHAIN PRECURSOR	0.024
509	U47322	Cloning vector DNA, complete sequence.	2.00E-38	COA1_SV40	COAT PROTEIN VP1	6.2
510	AF031924	Homo sapiens homeobox transcription factor barx2	e-156	CCMA_HAEIN	HEME EXPORTER PROTEIN A (CYTOCHROME C- TYPE BIOGENESIS ATP-BINDING PROTEIN CCMA)	3.5
511	AF010484	Homo sapiens ICI YAC 9IA12, right end sequence	3.00E-10	<none></none>	<none></none>	<none></none>
512	Z63829	H.sapiens CpG DNA, clone 90h2, forward read cpg90h2.ft1a.	5.00E-22	NFIR_MESAU	NUCLEAR FACTOR 1 CLONE PNF I/RED1 (NF-I) (CCAAT-BOX BINDING TRANSCRIPTION FACTOR) (CTF) (TGGCA-BINDING PROTEIN)	2.4
513		H.sapiens mRNA for SURF-2	5.00E-97	SUR2_HUMAN	SURFEIT LOCUS PROTEIN 2	1.00E-46
514		Xenopus laevis mitotic phosphoprotein 90 mRNA, complete cds	7.00E-06	<none></none>	<none></none>	<none></none>
515		Mouse mRNA for arylhydrocarbon receptor, complete cds	e-154	TEGU_EBV	LARGE TEGUMENT PROTEIN	3.4
516		Homo sapiens splicing factor (CC1.4) mRNA, complete cds.	e-117	<none></none>	<none></none>	<none></none>

Table 2

		eighbor (BlastN vs.	•	Nearest Neighbor (BlastX vs. Non-Redundant Proteins)			
SEQ	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE	
ID							
517	X17093	Human HLA-F gene for human leukocyte antigen F	0.009	YENI_SCHPO	oli on the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the con	5.4	
518	AB017026	Mus musculus mRNA for oxysterol-binding protein, complete cds	0	OXYB_HUMAN	OXYSTEROL- BINDING PROTEIN	1.00E-40	
519	X55038	Mouse mCENP-B gene for centromere autoantigen B	0.001	YNW7_YEAST	HYPOTHETICAL 68.8 KD PROTEIN IN URE2-SSU72 INTERGENIC REGION	3.00E-04	
520 .		Homo sapiens mRNA for KIAA0780 protein, partial cds	3.00E-41	LBR_CHICK	LAMIN B RECEPTOR	2.3	
521	U95094	Xenopus laevis XL-INCENP (XL-INCENP) mRNA, complete cds	1.00E-10	CA25_HUMAN	PROCOLLAGEN ALPHA 2(V) CHAIN PRECURSOR	0.002	
522	X03558	Human mRNA for elongation factor 1 alpha subunit	0	EF11_HUMAN	ELONGATION FACTOR 1-ALPHA 1 (EF-1-ALPHA-1)	e-110	
523		Xenopus laevis mitotic phosphoprotein 90 mRNA, complete cds	3.00E-11	_	HYPOTHETICAL 36.4 KD PROTEIN IN NUP116-FAR3 INTERGENIC REGION	8.00E-07	
524		Homo sapiens mRNA for KIAA0691 protein, complete cds	0	_	GENERAL NEGATIVE REGULATOR OF TRANSCRIPTION SUBUNIT 2	8.00E-05	
525		Homo sapiens DNA for TRKA, exon 17 and complete cds	0	_	HIGH AFFINITY NERVE GROWTH FACTOR RECEPTOR PRECURSOR PROTEIN) (P140- TRKA)	2.00E-27	

Table 2

	i e	ighbor (BlastN vs. 0	Genbank)		BlastX vs. Non-Redund	
1 1	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
ID						
526	U95102	Xenopus laevis mitotic phosphoprotein 90 mRNA, complete cds	5.00E-15	CNG4_BOVIN	240K PROTEIN OF ROD PHOTORECEPTOR CNG-CHANNEL CYCLIC-NUCLEOTIDE-GATED CATION CHANNEL 4 (CNG CHANNEL 4) MODULATORY SUBUNIT))	0.018
527	U95094	Xenopus laevis XL-INCENP (XL-INCENP) mRNA, complete cds	2.00E-06	HMZ1_DROME	ZERKNUELLT PROTEIN I (ZEN-1)	0.88
528	J03750	Mouse single stranded DNA binding protein p9 mRNA, complete cds.	e-135	P15_HUMAN	ACTIVATED RNA POLYMERASE II TRANSCRIPTIONA L COACTIVATOR P15 (PC4) (P14)	3.00E-21
529	U95094	Xenopus laevis XL-INCENP (XL-INCENP) mRNA, complete cds	1.00E-12	RS5_DROME	40S RIBOSOMAL PROTEIN S5	0.42
530	Z57610	H.sapiens CpG DNA, clone 187a10, reverse read cpg187a10.rt1a.	8.00E-61	HN3B_MOUSE	HEPATOCYTE NUCLEAR FACTOR 3-BETA (HNF-3B)	4.00E-15
531	U95760	Drosophila melanogaster strawberry notch (sno) mRNA, complete cds	3.00E-60	<none></none>	<none></none>	<none></none>
532	U95094	Xenopus laevis XL-INCENP (XL-INCENP) mRNA, complete cds	4.00E-11	<none></none>	<none></none>	<none></none>
533	U50535	Human BRCA2 region, mRNA sequence CG006	4.00E-12	ALU1_HUMAN	!!!! ALU SUBFAMILY J WARNING ENTRY !!!!	1.1
534	X92841	H.sapiens MICA gene	1.00E-55	LIN1_HUMAN	LINE-1 REVERSE TRANSCRIPTASE HOMOLOG	6.00E-09

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Table 2

		ighbor (BlastN vs. 0	Genbank)		BlastX vs. Non-Redund	
SEQ	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
ID						
535	U60337	Homo sapiens beta-mannosidase mRNA, complete cds	0	NODC_BRAEL	N- ACETYLGLUCOSA MINYLTRANSFER ASE (EC 2.4.1)	1.4
536	M21731	Human lipocortin- V mRNA, complete cds.	e-169	ANX5_HUMAN	ANNEXIN V (LIPOCORTIN V) (ENDONEXIN II) (CALPHOBINDIN I) (CBP-I) (PLACENTAL ANTICOAGULANT PROTEIN I) (PAP-I) ANTICOAGULANT -ALPHA) (VAC-ALPHA) (ANCHORIN CII)	1.00E-05
537	Y08013	S.salar DNA segment containing GT repeat	0.006	<none></none>	<none></none>	<none></none>
538	<none></none>	<none></none>	<none></none>	<none></none>	<none></none>	<none></none>
539	M98502	Mus musculus protein encoding twelve zinc finger proteins (pMLZ-4) mRNA, complete cds.	2.00E-17	DYNA_CHICK	DYNACTIN, 117 KD ISOFORM	7.4
540	U95102	Xenopus laevis mitotic phosphoprotein 90 mRNA, complete cds	6.00E-05	HXA3_HAEIN	HEME:HEMOPEXI N-BINDING PROTEIN PRECURSOR	2.6
541	U95094	Xenopus laevis XL-INCENP (XL-INCENP) mRNA, complete cds	1.00E-13	AMO_KLEAE	AMINE OXIDASE PRECURSOR (EC 1.4.3.6) (MONAMINE OXIDASE) (TYRAMINE OXIDASE)	1.5
542	AF083322	Homo sapiens centriole associated protein CEP110 mRNA, complete cds	e-133	CA34_HUMAN	PROCOLLAGEN ALPHA 3(IV) CHAIN PRECURSOR	1.5
543	J03746	Human glutathione S- transferase mRNA, complete cds.	e-170	GTMI_HUMAN	GLUTATHIONE S- TRANSFERASE, MICROSOMAL (EC 2.5.1.18)	5.00E-39

Table 2

	Nearest Ne	ighbor (BlastN vs. 0	Genbank)	Nearest Neighbor (E	BlastX vs. Non-Redund	
SEQ	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
ID						
544	U67522	Methanococcus jannaschii section 64 of 150 of the complete genome	0.37	A1AA_HUMAN	ALPHA-1A ADRENERGIC RECEPTOR	4.3
545	U95102	Xenopus laevis mitotic phosphoprotein 90 mRNA, complete cds	2.00E-07	<none></none>	<none></none>	<none></none>
546	<none></none>	<none></none>	<none></none>	<none></none>	<none></none>	<none></none>
547	<none></none>	<none></none>	<none></none>	<none></none>	<none></none>	<none></none>
548	D87001	Human (lambda) DNA for immunoglobulin light chain	0.35	VAL3_TYLCU	AL3 PROTEIN (C3 PROTEIN)	3.2
549	U95094	Xenopus laevis XL-INCENP (XL-INCENP) mRNA, complete cds	3.00E-08	TEGU_HSV11	LARGE TEGUMENT PROTEIN (VIRION PROTEIN UL36)	0.004
550	D16991	Human HepG2 partial cDNA, clone hmd2d01m5	8.00E-09	PTM1_YEAST	PROTEIN PTM1 PRECURSOR	0.033
551	M34025	Human fetal Ig heavy chain variable region	3.2	<none></none>	<none></none>	<none></none>
552	M98502	Mus musculus protein encoding twelve zinc finger proteins (pMLZ-4) mRNA, complete cds.	5.00E-14	<none></none>	<none></none>	<none></none>
553	U95098	Xenopus laevis mitotic phosphoprotein 44 mRNA, partial cds	0.002	<none></none>	<none></none>	<none></none>
554	Z78730	H.sapiens flow- sorted chromosome 6 HindIII fragment, SC6pA15C3	3.00E-20	ALU1_HUMAN	!!!! ALU SUBFAMILY J WARNING ENTRY !!!!	5.00E-06
555	U74496	Human chromosome 4q35 subtelomeric sequence	8.00E-08	ICP4_VZVD	TRANS-ACTING TRANSCRIPTIONA L PROTEIN ICP4	0.39

Table 2

		eighbor (BlastN vs.		Nearest Neighbor (BlastX vs. Non-Redund	lant Proteins)
SEQ	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
ID						
556	U39875	Rattus norvegicus EF-hand Ca2+- binding protein p22 mRNA, complete cds.	2.00E-56	YHFK_ECOLI	HYPOTHETICAL 79.5 KD PROTEIN IN CRP-ARGD INTERGENIC REGION (0696)	9.8
557	U65416	Human MHC class I molecule (MICB) gene, complete cds	0.12	<none></none>	<none></none>	<none></none>
558	AG000037	Homo sapiens genomic DNA, 21q region, clone: 9H11A22	5.00E-25	<none></none>	<none></none>	<none></none>
559	U95102	Xenopus laevis mitotic phosphoprotein 90 mRNA, complete cds	5.00E-05	<none></none>	<none></none>	<none></none>
560	AB007918	Homo sapiens mRNA for KIAA0449 protein, partial cds	0.015	VGLE_HSV11	GLYCOPROTEINE PRECURSOR	2.2
561	U58884	Mus musculus SH3-containing protein SH3P7 mRNA, complete cds. similar to Human Drebrin	1.00E-73	YCV2_YEAST	HYPOTHETICAL 13.8 KD PROTEIN IN PWP2-SUP61 INTERGENIC REGION	2.6
562	AB007878	Homo sapiens KIAA0418 mRNA, complete cds	e-110	GLU2_MAIZE	GLUTELIN 2 PRECURSOR (ZEIN-GAMMA) (27 KD ZEIN)	0.72
563	AF065482	Homo sapiens sorting nexin 2 (SNX2) mRNA, complete cds	0	YJD6_YEAST	HYPOTHETICAL 49.0 KD PROTEIN IN NSP1-KAR2 INTERGENIC REGION	1.4
564	U27873	Stealth virus 1 clone 3B11 T7	0.002	SYN1_HUMAN	SYNAPSINS IA AND IB (BRAIN PROTEIN 4.1)	1.6
565	L38951	Homo sapiens importin beta subunit mRNA, complete cds	2.00E-68	VP2_BRD	STRUCTURAL CORE PROTEIN VP2	1.1
566		Homo sapiens clone 23763 unknown mRNA, partial cds	e-165	YOHI_AZOVI	HYPOTHETICAL 33.2 KD PROTEIN IN IBPB 5'REGION	7.5

Table 2

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non-Redundant Proteins)			
`	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE	
ID							
567	Z56295	H.sapiens CpG	0.12	A1AB_CANFA	ALPHA-1B	0.85	
		DNA, clone 10c2, forward read			ADRENERGIC		
		cpg10c2.ft1a.			RECEPTOR		
568	Z83792	G.gallus	0.12	<none></none>	(FRAGMENT) <none></none>	<none></none>	
300	203772	microsatellite	0.12	\IVOIVL>	NONE	\NONE>	
		DNA (LEI0222					
569	U11820	Feline	1.1	<none></none>	<none></none>	<none></none>	
		immunodeficienc					
j		y virus					
		USIL2489_7B gag polyprotein					
		(gag) gene,					
		complete cds,					
		polymerase					
		polyprotein (pol)					
		gene, partial cds,					
		vif protein (vif), complete cds, and					
		envelope					
		glycoprotein					
		(env), complete					
570	1/10065	cds, complete g	6.0077.04				
570	M18065	Mouse 18S and 28S ribosomal	6.00E-04	CC40_YEAST	CELL DIVISION	3.7	
		DNA, 5'			CONTROL PROTEIN 40		
		hypervariable			I KOTEM 40		
		(Vr) region, clone					
		M1.					
571	AF053645	Homo sapiens	2.00E-07	YMQ4_CAEEL	HYPOTHETICAL	4.3	
		cellular apoptosis susceptibility			25.8 KD PROTEIN K02D10.4 IN		
		protein (CSE1)			CHROMOSOME III		
		gene, exons 3					
		through 10					
572	X04588	Human 2.5 kb	0	<none></none>	<none></none>	<none></none>	
		mRNA for cytoskeletal	l				
		tropomyosin					
		TM30(nm)					
573	AC001159	Homo sapiens	5.00E-04	XYND CELFI	ENDO-1,4-BETA-	7.3	
		(subclone 1_h9		_	XYLANASE D		
		from PAC H92)	ľ		PRECURSOR (EC		
		DNA sequence			3.2.1.8)		
574		H.sapiens CpG	4.00E-13	<none></none>	<none></none>	<none></none>	
		DNA, clone 2c10, forward read					
		cpg2c10.ft1aa.					
575		Homo sapiens	e-164	<none></none>	<none></none>	<none></none>	
	1	clone 24781			1101112	-11011L	
		<u></u>					

Table 2

	Nearest Ne	ighbor (BlastN vs.	Genbank)	Nearest Neighbor (BlastX vs. Non-Redunc	lant Proteins)
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
		mRNA sequence				
576	Y11306	Homo sapiens mRNA for hTCF- 4	2.00E-48	TCF1_HUMAN	T-CELL-SPECIFIC TRANSCRIPTION FACTOR 1 (TCF-1)	2.00E-15
577	X65279	pWE15 cosmid vector DNA	7.00E-69	OCLN_POTTR	Q28793 potorous tridactylus (potoroo). occludin. 11/98	0.71
578	M10296	Mouse DNA with homology to EBV IR3 repeat, segment 1, clone Mu2.	0.001	LMB1_HYDAT	LAMININ BETA-1 CHAIN PRECURSOR (FRAGMENTS)	1.9
579	X53744	Canine mRNA for 68kDA subunit of signal recognition particle (SRP68)	e-162	SR68_CANFA	SIGNAL RECOGNITION PARTICLE 68 KD PROTEIN (SRP68)	5.00E-16
580		Homo sapiens full length insert cDNA clone ZD80G11	2.00E-04	<none></none>	<none></none>	<none></none>
581	U15140	Mycobacterium bovis ribosomal proteins IF-1 complete cds, and S4 (rpsD) gene, partial cds	1.3	<none></none>	<none></none>	<none></none>
582		Human mRNA for ryudocan core protein	e-166	RSP4_ARATH	40S RIBOSOMAL PROTEIN SA (P40) (LAMININ RECEPTOR HOMOLOG)	1.4
583		neoplasm-related C140 product [human, thyroid carcinoma cells, mRNA, 670 nt]	9.00E-30	RL6_HUMAN	60S RIBOSÓMAL PROTEIN L6 (TAX- RESPONSIVE ENHANCER ELEMENT BINDING PROTEIN 107) (TAXREB107)	5.6
584		Anopheles gambiae complete mitochondrial genome	0.014	<none></none>	<none></none>	<none></none>
585		H.sapiens gene for chemokine HCC-1.	1.1	AMY1_DICTH	ALPHA-AMYLASE I (EC 3.2.1.1) (1,4- ALPHA-D- GLUCAN GLUCANOHYDRO LASE)	2.5

Table 2

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non-Redundant Proteins)			
SEQ	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE	
ID							
586	U95098	Xenopus laevis mitotic phosphoprotein 44 mRNA, partial cds	2.00E-04	<none></none>	<none></none>	<none></none>	
587	AF029893	Homo sapiens i- beta-1,3-N- acetylglucosamin yltransferase mRNA, complete cds	0.13	HEMO_PIG	HEMOPEXIN PRECURSOR (HYALURONIDAS E) (EC 3.2.1.35)	3.5	
588	J05109	T.thermophila calcium-binding 25 kDa (TCBP 25) protein gene, complete cds.	0.014	<none></none>	<none></none>	<none></none>	
589	U95098	Xenopus laevis mitotic phosphoprotein 44 mRNA, partial cds	6.00E-04	<none></none>	<none></none>	<none></none>	
590	AF060246	Mus musculus strain C57BL/6 zinc finger protein 106 (Zfp106) mRNA, H3a-a allele, complete cds	1.00E-83	SCRB_PEDPE	SUCROSE-6- PHOSPHATE HYDROLASE (EC 3.2.1.26) (SUCRASE)	10	
591	Y11966	B.aphidicola (host T.suberi) plasmid pBTs1 genes leuA, hspA, repA2, repA1, leuB, leuC, leuD, leuA	0.37	<none></none>	<none></none>	<none></none>	
592	U20428	Human SNC19 mRNA sequence	1.00E-64	YY22_MYCTU	HYPOTHETICAL 30.8 KD PROTEIN CY49.22	0.29	
593	AF043084	Lycopersicon esculentum ethylene receptor homolog (ETR1) mRNA, complete cds	0.37	KNIR_DROME	ZYGOTIC GAP PROTEIN KNIRPS	9.9	
594	X65279	pWE15 cosmid vector DNA	5.00E-66	COA1_SV40	COAT PROTEIN VP1	0.001	
595	U95098	Xenopus laevis mitotic phosphoprotein 44 mRNA, partial	0.041	UL88_HSV7J	PROTEIN U59	5.8	

Table 2

		eighbor (BlastN vs.	Genbank)	Nearest Neighbor (BlastX vs. Non-Redunc	lant Proteins)
SEQ	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
ID						
		cds				
596	M91452	Sus scrofa	3.2	AIONES	ALON ITS	210215
370	10191432	ryanodine	3.2	<none></none>	<none></none>	<none></none>
		receptor (RYR1)				
		gene, complete				
597	U77327	cds. Human Ki-1/57	150	0.171.017		
391	0//32/	intracellular	e-158	GAT1_CHICK	ERYTHROID TRANSCRIPTION	1.2
		antigen mRNA,			FACTOR (GATA-1)	
		partial cds			(ERYF1)	
598	U77327	Human Ki-1/57	0	RPB7_ARATH	DNA-DIRECTED	6.2
		intracellular antigen mRNA,			RNA POLYMERASE II	
		partial cds			19 KD	
		ļ [*]			POLYPEPTIDE (EC	
					2.7.7.6) (RNA	
					POLYMERASE II	
599	Y16964	Saccharomyces	0.37	NMD5 YEAST	SUBUNIT 5) NONSENSE-	1.9
		sp. mitochondrial	0.57	111100_101	MEDIATED MRNA	1.9
		DNA for OLI1			DECAY PROTEIN 5	
600	U95102	gene, strain CID1	C 0 0 E 0 C	A LOND	210210	
000	093102	Xenopus laevis mitotic	6.00E-06	<none></none>	<none></none>	<none></none>
		phosphoprotein				
		90 mRNA,				
(01	1105000	complete cds	0.000.00	NONE		
601	U95098	Xenopus laevis mitotic	8.00E-08	<none></none>	<none></none>	<none></none>
		phosphoprotein				
		44 mRNA, partial				
602	A F001046	cds		DUIG BOXES		
602	AF091046	Brugia pahangi nuclear hormone	1.1	INVO_PONPY	INVOLUCRIN	0.23
		receptor (bhr-1)				
		gene, partial cds				
603	M87339	Human	0	AC12_HUMAN	ACTIVATOR 1 37	1.00E-38
		replication factor C, 37-kDa subunit			KD SUBUNIT	
		mRNA, complete			(REPLICATION FACTOR C 37 KD	ļ
		cds			SUBUNIT) (A1 37	
					KD SUBUNIT) (RF-	
			Ī		C 37 KD SUBUNIT)	
604	D28116	Human genes for	0.39	<none></none>	(RFC37) <none></none>	<none></none>
		collagen type IV	0.57	TIONE	NIONE	-NONE/
		alpha 5 and 6,				
		exon 1 and exon				
			26			

Table 2

	Nearest Ne	ighbor (BlastN vs.	Genbank)	Nearest Neighbor (I	BlastX vs. Non-Redund	ant Proteins)
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
		1'				
605	U95102	Xenopus laevis mitotic phosphoprotein 90 mRNA, complete cds	2.00E-06	<none></none>	<none></none>	<none></none>
606	AE001149	Borrelia burgdorferi (section 35 of 70) of the complete genome	0.13	<none></none>	<none></none>	<none></none>
607	X14168	Human pLC46 with DNA replication origin	6.00E-16	Z136_HUMAN	ZINC FINGER PROTEIN 136	0.31
608	Z57610	H.sapiens CpG DNA, clone 187a10, reverse read cpg187a10.rt1a.	7.00E-90	HN3B_RAT	HEPATOCYTE NUCLEAR FACTOR 3-BETA (HNF-3B)	1.00E-19
609	U95098	Xenopus laevis mitotic phosphoprotein 44 mRNA, partial cds	0.043	PGCV_MOUSE	VERSICAN CORE PROTEIN PRECURSOR (LARGE FIBROBLAST PROTEOGLYCAN) (CHONDROITIN SULFATE PROTEOGLYCAN CORE PROTEIN 2) (PG-M)	3.5
610	U95094	Xenopus laevis XL-INCENP (XL-INCENP) mRNA, complete cds	7.00E-07	CA11_CHICK	PROCOLLAGEN ALPHA 1(I) CHAIN PRECURSOR	0.4
611		Homo sapiens mRNA, chromosome 1 specific transcript KIAA0487	e-106	RRPB_CVMA5	RNA-DIRECTED RNA POLYMERASE (EC 2.7.7.48) (ORF1B)	9.7
612	U95102	Xenopus laevis mitotic phosphoprotein 90 mRNA, complete cds	0.005	<none></none>	<none></none>	<none></none>

Table 2

		ighbor (BlastN vs. 0		,	BlastX vs. Non-Redund	
SEQ	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
ID						
613	U95094	Xenopus laevis XL-INCENP (XL-INCENP) mRNA, complete cds	6.00E-05	UL52_EBV	HELICASE/PRIMA SE COMPLEX PROTEIN (PROBABLE DNA REPLICATION PROTEIN BSLF1)	5.9
614	U95760	Drosophila melanogaster strawberry notch (sno) mRNA, complete cds	3.00E-71	POLG_PVYHU	GENOME POLYPROTEIN (CONTAINS: N- TERMINAL PROTEIN; HELPER COMPONENT PROTEINASE (EC 3.4.22) (HC-PRO); 42-50 KD PROTEIN; CYTOPLASMIC INCLUSION PROTEIN (CI); 6 KD PROTEIN; NUCLEAR INCLUSION PROTEIN A (NI- A) (EC 3.4.22) (49K PROTEINASE) (49	4.3
615	U95102	Xenopus laevis mitotic phosphoprotein 90 mRNA, complete cds	9.00E-09	VP3_ROTPC	INNER CORE PROTEIN VP3	7.7
616	J05499	Rattus norvegicus L-glutamine amidohydrolase mRNA, complete cds	e-143	GLSL_RAT	GLUTAMINASE, LIVER ISOFORM PRECURSOR (EC 3.5.1.2) (GLS)	7.00E-67
617	M19262	Rat clathrin light chain (LCB3) mRNA, complete cds.	0.37	Y642_METJA	HYPOTHETICAL PROTEIN MJ0642	5.8
618	M21191	Human aldolase pseudogene mRNA, complete cds.	1.00E-32	LINI_NYCCO	LINE-1 REVERSE TRANSCRIPTASE HOMOLOG	6.00E-17
619	. U95094	Xenopus laevis XL-INCENP (XL-INCENP) mRNA, complete cds	1.00E-11	NUCM_BOVIN	NADH- UBIQUINONE OXIDOREDUCTAS E 49 KD SUBUNIT (EC 1.6.5.3) (EC 1.6.99.3) (COMPLEX I- 49KD) (CI-49KD)	0.044

Table 2

	Nearest Ne	ighbor (BlastN vs. 0	Genbank)	Nearest Neighbor (E	BlastX vs. Non-Redund	
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
620	U95098	Xenopus laevis mitotic phosphoprotein 44 mRNA, partial cds	0.005	HEMZ_RHOCA	FERROCHELATAS E (EC 4.99.1.1) (PROTOHEME FERRO-LYASE)	4.4
621		Homo sapiens ribosomal protein s4 X isoform gene, complete cds	0.002	<none></none>	<none></none>	<none></none>
622	X07158	Chironomus thummi DNA for Cla repetitive element	0.13	<none></none>	<none></none>	<none></none>
623	U95094	Xenopus laevis XL-INCENP (XL-INCENP) mRNA, complete cds	8.00E-04	<none></none>	<none></none>	<none></none>
624	AF100470	Rattus norvegicus ribosome attached membrane protein 4 (RAMP4) mRNA, complete cds	1.00E-53	<none></none>	<none></none>	<none></none>
625		Human nuclear factor I-B2 (NFIB2) mRNA, complete cds	2.00E-38	<none></none>	<none></none>	<none></none>
626	M13452	Human lamin A mRNA, 3'end.	6.00E-16	<none></none>	<none></none>	<none></none>
627	U95094	Xenopus laevis XL-INCENP (XL-INCENP) mRNA, complete cds	0.014	ACDV_RAT	ACYL-COA DEHYDROGENAS E, VERY-LONG- CHAIN SPECIFIC PRECURSOR (EC 1.3.99) (VLCAD)	4.00E-20
628	U95094	Xenopus laevis XL-INCENP (XL-INCENP) mRNA, complete cds	3.00E-10	<none></none>	<none></none>	<none></none>
629	<none></none>	<none></none>	<none></none>	<none></none>	<none></none>	<none></none>
630	U95102	Xenopus laevis mitotic phosphoprotein 90 mRNA, complete cds	2.00E-05	<none></none>	<none></none>	<none></none>

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Table 2

		ighbor (BlastN vs. 6	Genbank)		BlastX vs. Non-Redund	
SEQ	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
ID						
631	U95102	Xenopus laevis mitotic phosphoprotein 90 mRNA, complete cds	6.00E-05	<none></none>	<none></none>	<none></none>
632	U95094	Xenopus laevis XL-INCENP (XL-INCENP) mRNA, complete cds	6.00E-05	YS83_CAEEL	HYPOTHETICAL 86.9 KD PROTEIN ZK945.3 IN CHROMOSOME II	0.65
633	U95102	Xenopus laevis mitotic phosphoprotein 90 mRNA, complete cds	3.00E-09	NRP_MOUSE	NEUROPILIN PRECURSOR (A5 PROTEIN)	2.7
634	U95098	Xenopus laevis mitotic phosphoprotein 44 mRNA, partial cds	2.00E-05	Y4JN_RHISN	HYPOTHETICAL 16.3 KD PROTEIN Y4JN	5.9
635	U95102	Xenopus laevis mitotic phosphoprotein 90 mRNA, complete cds	6.00E-05	<none></none>	<none></none>	<none></none>
636	X64707	H.sapiens BBC1 mRNA	e-179	RL13_HUMAN	60S RIBOSOMAL PROTEIN L13 (BREAST BASIC CONSERVED PROTEIN 1)	5.00E-40
637	U95102	Xenopus laevis mitotic phosphoprotein 90 mRNA, complete cds	3.00E-08	. <none></none>	<none></none>	<none></none>
638	X14168	Human pLC46 with DNA replication origin	5.00E-14	SP3_HUMAN	TRANSCRIPTION FACTOR SP3 (SPR- 2) (FRAGMENT)	0.19
639	X90999	H.sapiens mRNA for Glyoxalase II	9.00E-20	GLO2_HUMAN	HYDROXYACYLG LUTATHIONE HYDROLASE (EC 3.1.2.6)	0.007
640	AF083322	Homo sapiens centriole associated protein CEP110 mRNA, complete cds	9.00E-51	KIF4_MOUSE	KINESIN-LIKE PROTEIN KIF4	0.005

Table 2

		eighbor (BlastN vs. C	Genbank)	Nearest Neighbor (B	BlastX vs. Non-Redund	
1 1	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
ID						
641	Z12002	M.musculus Pvt-1 mRNA.	0.36	CP5F_CANTR	CYTOCHROME P450 LIIA6 (ALKANE- INDUCIBLE) (EC 1.14.14.1) (P450- ALK3)	5.6
642	M10206	R.sphaeroides reaction center L subunit (complete cds) and M subunit (5' end) genes.	1.1	YGR1_YEAST	HYPOTHETICAL 34.8 KD PROTEIN IN SUT1-RCK1 INTERGENIC REGION	0.006
643	K02668	E. coli ddl gene encoding D- alanine:D-alanine ligase and ftsQ and ftsA genes, complete cds, and ftsZ gene, 5' end.	3.3	ANKB_HUMAN	ANKYRIN, BRAIN VARIANT 1 (ANKYRIN B) (ANKYRIN, NONERYTHROID)	7.00E-07
644	<none></none>	<none></none>	<none></none>	<none></none>	<none></none>	<none></none>
645	X53616	C.domesticus calnexin (pp90) mRNA	1.1	<none></none>	<none></none>	<none></none>
646	X57010	Human COL2A1 gene for collagen II alpha 1 chain, exons E2-E15	3.3	PRIO_PIG	MAJOR PRION PROTEIN PRECURSOR (PRP)	1.9
647	U95097	Xenopus laevis mitotic phosphoprotein 43 mRNA, partial cds	1.1	UL07_HSV2H	PROTEIN UL7	7.3
648	X52956	Human CAMII- psi3 calmodulin retropseudogene	0.37	PRTP_EBV	PROBABLE PROCESSING AND TRANSPORT PROTEIN	7.5
649	M93425	Human protein tyrosine phosphatase (PTP-PEST) mRNA, complete cds.	0	PTNC_HUMAN	PROTEIN- TYROSINE PHOSPHATASE G1 (EC 3.1.3.48) (PTPG1)	e-107
650	L47615	Mus musculus DNA-binding protein (Fli-1) gene, 5' end of cds.	0.13	YA53_SCHPO	HYPOTHETICAL 24.2 KD PROTEIN C13A11.03 IN CHROMOSOME I	2.00E-07
651	U60337	Homo sapiens beta-mannosidase mRNA, complete	0	GIL1_ENTHI	GALACTOSE- INHIBITABLE LECTIN 170 KD	0.22

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Table 2

		ighbor (BlastN vs. (Genbank)		BlastX vs. Non-Redunda	
_ `	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
ID						
		cds			SUBUNIT	
652	U08813	Oryctolagus cuniculus	1.00E-22	NAG1_HUMAN	SODIUM/GLUCOS E	0.1
		Na+/glucose cotransporter- related protein			COTRANSPORTER 1 (NA(+)/GLUCOSE COTRANSPORTER	
		mRNA, complete cds.			1) (HIGH AFFINITY	
					SODIUM- GLUCOSE	
					COTRANSPORTER	
653	Y00282	Human mRNA	2.00E-78	RIB2 HUMAN	DOLICHYL-	5.00E-19
033		for ribophorin II	2.000-78	KID2_HOMAN	DIPHOSPHOOLIG	3.00L-19
					OSACCHARIDE PROTEIN	
					GLYCOSYLTRANS	
					FERASE 63 KD	
					SUBUNIT	
					PRECURSOR (EC 2.4.1.119)	
					(RIBOPHORIN II)	
654	D10051	Human gene for 92-kDa type IV	0.014	TAGB_DICDI	PRESTALK- SPECIFIC	7.6
		collagenase, 5'-			PROTEIN TAGB	
		flanking region			PRECURSOR (EC	
(5.5	1.00000		0.000.00	AIONES	3.4.21)	ALONES
655	M29930	Human insulin receptor (allele 2)	8.00E-08	<none></none>	<none></none>	<none></none>
		gene, exons 14, 15, 16 and 17.				
656	U78310	Homo sapiens pescadillo	0	YG2S_YEAST	HYPOTHETICAL 69.9 KD PROTEIN	0.002
		mRNA, complete			IN MIC1-SRB5	
		cds			INTERGENIC REGION	
657		S.coelicolor	3.2	YBS0_YEAST	HYPOTHETICAL	0.073
		A3(2) promoter sequence pth270			27.0 KD PROTEIN IN VAL1-HSP26	
		pina, o			INTERGENIC	
					REGION	
658	U50535	Human BRCA2 region, mRNA	4.00E-12	ALU1_HUMAN	!!!! ALU SUBFAMILY J	1.2
		sequence CG006			WARNING ENTRY	
		1			1111	

Table 2

	Nearest Ne	ighbor (BlastN vs. 0	Genbank)		BlastX vs. Non-Redund	
SEQ	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
ID						
659	U15522	Sus scrofa clone pvg1a Ig heavy chain variable VDJ region mRNA, partial cds.	3.2	Z165_HUMAN	ZINC FINGER PROTEIN 165	3.2
660	M20918	C.thummi piger haemoglobin (Hb) gene DNA, complete cds.	0.12	YT25_CAEEL	HYPOTHETICAL 59.9 KD PROTEIN B0304.5 IN CHROMOSOME II	0.033
661	U60337	Homo sapiens beta-mannosidase mRNA, complete cds	0	<none></none>	<none></none>	<none></none>
662	U95098	Xenopus laevis mitotic phosphoprotein 44 mRNA, partial cds	0.001	ENV_MLVFP	ENV POLYPROTEIN PRECURSOR (CONTAINS: KNOB PROTEIN GP70; SPIKE PROTEIN P15E; R PROTEIN)	3.3
663	M97287	Human MAR/SAR DNA binding protein (SATB1) mRNA, complete cds. > :: gb I58691 I58691 Sequence 1 from patent US 5652340	0	SAT1_HUMAN	DNA-BINDING PROTEIN SATB1 (SPECIAL AT-RICH SEQUENCE BINDING PROTEIN 1)	2.00E-20
664	L42612	Homo sapiens keratin 6 isoform K6f (KRT6F) mRNA, complete cds	e-168	K2C4_BOVIN	KERATIN, TYPE II CYTOSKELETAL 59 KD, COMPONENT IV	4.00E-10
665	U17901	Rattus norvegicus phospholipase A- 2-activating protein (plap) mRNA, complete cds.	e-152	PLAP_MOUSE	PHOSPHOLIPASE A-2-ACTIVATING PROTEIN (PLAP)	4.00E-13
666	M73047	Homo sapiens tripeptidyl peptidase II mRNA, complete cds.	0	MERT_STRLI	MERCURIC TRANSPORT PROTEIN (MERCURY ION TRANSPORT PROTEIN)	4.4

Table 2

		ighbor (BlastN vs. (,		BlastX vs. Non-Redund	
1	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
ID				14.00		
667	U09954	Human ribosomal protein L9 gene, 5' region and complete cds.	0	RL9_HUMAN	60S RIBOSOMAL PROTEIN L9	2.00E-11
668	X98330	H.sapiens mRNA for ryanodine receptor 2	1.1	HS74_MOUSE	HEAT SHOCK 70 KD PROTEIN AGP- 2	0.034
669	U95094	Xenopus laevis XL-INCENP (XL-INCENP) mRNA, complete cds	0.002	RPC2_DROME	DNA-DIRECTED RNA POLYMERASE III 128 KD POLYPEPTIDE	1.1
670		Homo sapiens okadaic acid-inducible phosphoprotein (OA48-18) mRNA, complete cds	7.00E-80	LEGB_PEA	LEGUMIN B (FRAGMENT)	0.011
671	Z71419	S.cerevisiae chromosome XIV reading frame ORF YNL143c	1.1	FOCD_ECOLI	OUTER MEMBRANE USHER PROTEIN FOCD PRECURSOR	9.7
672	AF044965	Homo sapiens polio virus related protein 2 gene, alpha isoform, exon 6 and partial cds	e-167	PVR_MOUSE	POLIOVIRUS RECEPTOR HOMOLOG PRECURSOR	1.00E-12
673	X65319	Cloning vector pCAT-Enhancer	2.00E-80	S106_HUMAN	CALCYCLIN (PROLACTIN RECEPTOR ASSOCIATED PROTEIN) CALCIUM- BINDING PROTEIN A6)	3.00E-15
674	D29655	Pig mRNA for UMP-CMP kinase, complete cds	e-103	V319_ASFB7	J319 PROTEIN	4.3
675	U95094	Xenopus laevis XL-INCENP (XL-INCENP) mRNA, complete cds	8.00E-08	VEGR_RAT	VASCULAR ENDOTHELIAL GROWTH FACTOR RECEPTOR 1 PRECURSOR RECEPTOR FLT) (FLT-1)	3.3

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Table 2

	Nearest Ne	ighbor (BlastN vs. (Genbank)	Nearest Neighbor (E	BlastX vs. Non-Redund	ant Proteins)
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
676		S. cerevisiae gene for YmL33, mitochondrial ribosomal proteins of large subunit	2.00E-07	MALY_ECOLI •	MALY PROTEIN (EC 2.6.1)	5.6
677		Homo sapiens cofactor A protein mRNA, complete cds	e-160	TICA_MOUSE	TCP1- CHAPERONIN COFACTOR A	4.00E-19
678	Z96950	Gorilla gorilla DNA sequence orthologous to the human Xp:Yp telomere-junction region	5.00E-14	YHBZ_ECOLI	HYPOTHETICAL 43.3 KD GTP- BINDING PROTEIN IN DACB-RPMA INTERGENIC REGION (F390)	3.3
679	D50418	Mouse mRNA for AREC3, partial cds	2.00E-79	CYGX_RAT	OLFACTORY GUANYLYL CYCLASE GC-D PRECURSOR (EC 4.6.1.2)	1.1
680	Ú95098	Xenopus laevis mitotic phosphoprotein 44 mRNA, partial cds	8.00E-08	P2C2_SCHPO	PROTEIN PHOSPHATASE 2C HOMOLOG 2 (EC 3.1.3.16)	1.00E-04
681	AL010280	Plasmodium falciparum DNA *** SEQUENCING IN PROGRESS *** from contig 4-106, complete sequence	0.12	<none></none>	<none></none>	<none></none>
682	U95094	Xenopus laevis XL-INCENP (XL-INCENP) mRNA, complete cds	5.00E-04	VSM2_TRYBB	VARIANT SURFACE GLYCOPROTEIN MITAT 1.2 PRECURSOR (VSG 221)	4.3
683	U00238	Homo sapiens glutamine PRPP amidotransferase (GPAT) mRNA, complete cds	0	<none></none>	<none></none>	<none></none>
684	U95102	Xenopus laevis mitotic phosphoprotein 90 mRNA, complete cds	0.005	PRPR_SALTY	PROPIONATE CATABOLISM OPERON REGULATORY PROTEIN	1.5

Table 2

		ighbor (BlastN vs. 0			BlastX vs. Non-Redund	
	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
ID						
685	U95102	Xenopus laevis mitotic phosphoprotein 90 mRNA, complete cds	7.00E-07	YAND_SCHPO	HYPOTHETICAL 30.4 KD PROTEIN C3H1.13 IN CHROMOSOME I	0.38
686	D25538	Human mRNA for KIAA0037 gene, complete cds	0	<none></none>	<none></none>	<none></none>
687	U95102	Xenopus laevis mitotic phosphoprotein 90 mRNA, complete cds	2.00E-07	A1AA_RAT	ALPHA-1A ADRENERGIC RECEPTOR (RA42)	4.4
688	L26956	Mesocricetus auratus stearyl- CoA desaturase sequence including male hormone dependent gene derived from hamster frankorgan	4.00E-33	<none></none>	<none></none>	<none></none>
689	U95102	Xenopus laevis mitotic phosphoprotein 90 mRNA, complete cds	3.00E-10	<none></none>	<none></none>	<none></none>
690	U95102	Xenopus laevis mitotic phosphoprotein 90 mRNA, complete cds	3.00E-09	YO93_CAEEL	HYPOTHETICAL 58.5 KD PROTEIN T20B12.3 IN CHROMOSOME III	2.00E-08
691	U95102	Xenopus laevis mitotic phosphoprotein 90 mRNA, complete cds	8.00E-09	<none></none>	<none></none>	<none></none>
692	AB017026	Mus musculus mRNA for oxysterol-binding protein, complete cds	0	OXYB_RABIT	OXYSTEROL- BINDING PROTEIN	1.00E-34
693	U950 9 8	Xenopus laevis mitotic phosphoprotein 44 mRNA, partial cds	6.00E-04	UFO2_MAIZE	FLAVONOL 3-O- GLUCOSYLTRANS FERASE (EC 2.4.1.91)	3.1

Table 2

	î .	ighbor (BlastN vs. 0			BlastX vs. Non-Redund	
SEQ	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
ID						ļ
694	U95102	Xenopus laevis mitotic phosphoprotein 90 mRNA, complete cds	5.00E-04	<none></none>	<none></none>	<none></none>
695	U34954	Caenorhabditis elegans cyclophilin isoform 10	5.00E-24	CYPA_CAEEL	PEPTIDYL- PROLYL CIS- TRANS ISOMERASE 10 (EC 5.2.1.8)	2.00E-29
696		Homo sapiens mRNA for KIAA0595 protein, partial cds	0	RFX5_HUMAN	BINDING REGULATORY FACTOR	2.1
697		Human GS2 mRNA, complete cds.	2.00E-28	SKD1_MOUSE	SKD1 PROTEIN	4.00E-17
698	AF086275	Homo sapiens full length insert cDNA clone ZD45C02	3.00E-41	SPT7_YEAST	TRANSCRIPTIONA L ACTIVATOR SPT7	0.82
699	U95102	Xenopus laevis mitotic phosphoprotein 90 mRNA, complete cds	3.00E-10	CA1E_HUMAN	COLLAGEN ALPHA 1(XV) CHAIN PRECURSOR	1.1
700	U95102	Xenopus laevis mitotic phosphoprotein 90 mRNA, complete cds	4.00E-11	E434_ADECC	Q65962 canine adenovirus type 1 (strain cll). early e4 31 kd protein. 11/98	4.4
701		Drosophila melanogaster germline transcription factor gene, complete cds.	3.3	CISY_TETTH	CITRATE SYNTHASE, MITOCHONDRIAL PRECURSOR (EC 4.1.3.7) (14 NM FILAMENT- FORMING PROTEIN)	9.7
702	X58170	M.musculus mRNA for t- Complex Tcp-10a gene	2.00E-45	PME2_LYCES	PECTINESTERASE 2 PRECURSOR (EC 3.1.1.11) (PECTIN METHYLESTERAS E) (PE 2)	7.4
703	Z96207	H.sapiens telomeric DNA sequence, clone 12PTEL049, read 12PTELOO049.se	8.00E-08	<none></none>	<none></none>	<none></none>

Table 2

		ighbor (BlastN vs.			lastX vs. Non-Redund	ant Proteins)
SEQ	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
ID						
		q				
704	X58430	Human Hox1.8 gene	e-146	HXAA_HUMAN	HOMEOBOX PROTEIN HOX-A10 (HOX-1H) (HOX- 1.8) (PL)	4.00E-05
705	U95094	Xenopus laevis XL-INCENP (XL-INCENP) mRNA, complete cds	6.00E-06	YN39_SYNP7	HYPOTHETICAL 9.2 KD PROTEIN IN CYST-CYSR INTERGENIC REGION (ORF 81)	0.89
706	U95094	Xenopus laevis XL-INCENP (XL-INCENP) mRNA, complete cds	1.00E-11	MYSH_BOVIN	MYOSIN I HEAVY CHAIN-LIKE PROTEIN (MIHC) (BRUSH BORDER MYOSIN I) (BBMI)	0.001
707	M19961	Human cytochrome c oxidase subunit Vb (coxVb) mRNA, complete cds.	e-123	OTHU5B	<none></none>	3.00E-30
708	X68380	M.musculus gene for cathepsin D, exon 3	5.00E-04	42_MOUSE	ERYTHROCYTE MEMBRANE PROTEIN BAND 4.2 (P4.2) (PALLIDIN)	9.9
709	U95102	Xenopus laevis mitotic phosphoprotein 90 mRNA, complete cds	1.00E-11	TCPA_DROME	T-COMPLEX PROTEIN 1, ALPHA SUBUNIT (TCP-1-ALPHA)	4.3
710		Xenopus laevis mitotic phosphoprotein 90 mRNA, complete cds	3.00E-10	<none></none>	<none></none>	<none></none>
711	U95094	Xenopus laevis XL-INCENP (XL-INCENP) mRNA, complete cds	4.00E-12	<none></none>	<none></none>	<none></none>
712	U95102	Xenopus laevis mitotic phosphoprotein 90 mRNA, complete cds	0.002	<none></none>	<none></none>	<none></none>

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Table 2

		ighbor (BlastN vs. 0	Genbank)		BlastX vs. Non-Redund	
1	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
ID					***************************************	
713	AB018323	Homo sapiens mRNA for KIAA0780 protein, partial cds	3.00E-41	LBR_CHICK	LAMIN B RECEPTOR	3.4
714	U95102	Xenopus laevis mitotic phosphoprotein 90 mRNA, complete cds	6.00E-06	YM8L_YEAST	HYPOTHETICAL 71.1 KD PROTEIN IN DSK2-CAT8 INTERGENIC REGION	3,00E-08
715	U95102	Xenopus laevis mitotic phosphoprotein 90 mRNA, complete cds	4.00E-13	PSC_DROME	POSTERIOR SEX COMBS PROTEIN	0.6
716	L28101	Homo sapiens kallistatin (PI4) gene, exons 1-4, complete cds	7.00E-07	IRKX_RAT	INWARD RECTIFIER POTASSIUM CHANNEL BIR9 (KIR5.1)	5.4
717	AC001038	Homo sapiens (subclone 2_h2 from P1 H49) DNA sequence	8.00E-09	MGMT_YEAST	METHYLATED- DNAPROTEIN- CYSTEINE METHYLTRANSFE RASE	0.48
718	U95094	Xenopus laevis XL-INCENP (XL-INCENP) mRNA, complete cds	1.00E-11	YWDE_BACSU	HYPOTHETICAL 19.9 KD PROTEIN IN SACA-UNG INTERGENIC REGION PRECURSOR	1.8
719	U01139	Mus musculus B6D2F1 clone 2C11B mRNA.	e-110	GSC_DROME	HOMEOBOX PROTEIN GOOSECOID	7.2
720		Homo sapiens mRNA for kinesin-like DNA binding protein, complete cds	0	YBAV_ECOLI	HYPOTHETICAL 12.7 KD PROTEIN IN HUPB-COF INTERGENIC REGION	0.17
721	U95094	Xenopus laevis XL-INCENP (XL-INCENP) mRNA, complete cds	0.001	CPCF_SYNP2	PHYCOCYANOBIL IN LYASE BETA SUBUNIT (EC 4)	2.4
722	U95102	Xenopus laevis mitotic phosphoprotein 90 mRNA, complete cds	9.00E-10	<none></none>	<none></none>	<none></none>

Table 2

		ighbor (BlastN vs. 0	Genbank)	Nearest Neighbor (E	BlastX vs. Non-Redund	
SEQ	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
ID						
723	U95102	Xenopus laevis mitotic phosphoprotein 90 mRNA, complete cds	0.04	YKK7_CAEEL	HYPOTHETICAL 54.9 KD PROTEIN C02F5.7 IN CHROMOSOME III	0.057
724	U95094	Xenopus laevis XL-INCENP (XL-INCENP) mRNA, complete cds	8.00E-08	H5_CAIMO	HISTONE H5	0.39
725	U95094	Xenopus laevis XL-INCENP (XL-INCENP) mRNA, complete cds	3.00E-09	DED1_YEAST	PUTATIVE ATP- DEPENDENT RNA HELICASE DED1	0.5
726	J04617	Human elongation factor EF-1-alpha gene, complete cds. > :: dbj E02629 E0262 9 DNA of human polypeptide chain elongation factor-1 alpha	5.00E-36	ALU7_HUMAN	!!!! ALU SUBFAMILY SQ WARNING ENTRY !!!!	0.84
727	X54859	Porcine TNF- alpha and TNF- beta genes for tumour necrosis factors alpha and beta, respectively.	3.3	Z165_HUMAN	ZINC FINGER PROTEIN 165	5.6
728	D49911	Thermus thermophilus UvrA gene, complete cds	0.014	CC48_CAPAN	CELL DIVISION CYCLE PROTEIN 48 HOMOLOG	9.9
729	U95098	Xenopus laevis mitotic phosphoprotein 44 mRNA, partial cds	2.00E-06	CA25_HUMAN	PROCOLLAGEN ALPHA 2(V) CHAIN PRECURSOR	0.011
730	D15057	Human mRNA for DAD-1, complete cds	0	DAD1_HUMAN	DEFENDER AGAINST CELL DEATH 1 (DAD-1)	8.00E-16
731	U95098	Xenopus laevis mitotic phosphoprotein 44 mRNA, partial cds	6.00E-06	ANFD_RHOCA	NITROGENASE IRON-IRON PROTEIN ALPHA CHAIN (EC 1.18.6.1) (NITROGENASE COMPONENT I) (DINITROGENASE	9.6

Table 2

	Nearest Ne	ighbor (BlastN vs. 0	Genbank)		BlastX vs. Non-Redund	
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
732	U95098	Xenopus laevis mitotic phosphoprotein 44 mRNA, partial cds	7.00E-07	EFTU_CHLVI	ELONGATION FACTOR TU (EF- TU)	2.5
733	AB018335	Homo sapiens mRNA for KIAA0792 protein, complete cds	0	TRYM_RAT	MAST CELL TRYPTASE PRECURSOR (EC 3.4.21.59)	5.6
734	X98743	H.sapiens mRNA for RNA helicase (Myc-regulated dead box protein)	0.04	<none></none>	<none></none>	<none></none>
735	U95098	Xenopus laevis mitotic phosphoprotein 44 mRNA, partial cds	2.00E-07	<none></none>	<none></none>	<none></none>
736	Z49314	S.cerevisiae chromosome X reading frame ORF YJL039c	3.2	<none></none>	<none></none>	<none></none>
737	D12646	Mouse kif4 mRNA for microtubule- based motor protein KIF4, complete cds	0	KIF4_MOUSE	KINESIN-LIKE PROTEIN KIF4	2.00E-76
738	J04038	Human glyceraldehyde-3- phosphate dehydrogenase	2.00E-47	SDC1_HUMAN	SYNDECAN-1 PRECURSOR (SYND1) (CD138)	3.5
739	AF010238	Homo sapiens von Hippel- Lindau tumor suppressor	1.00E-09	LIN1_HUMAN	LINE-1 REVERSE TRANSCRIPTASE HOMOLOG	0.001
740	U95102	Xenopus laevis mitotic phosphoprotein 90 mRNA, complete cds	2.00E-06	YQJX_BACSU	HYPOTHETICAL 13.2 KD PROTEIN IN GLNQ-ANSR INTERGENIC REGION	9.9

Table 2

	Nearest Ne	ighbor (BlastN vs. 6	Genbank)	Nearest Neighbor (B	BlastX vs. Non-Redund	ant Proteins)
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
741	L21186	Human lysyl oxidase-like protein mRNA, complete cds.	e-145	OXRTL	<none></none>	1.00E-34
742	U95094	Xenopus laevis XL-INCENP (XL-INCENP) mRNA, complete cds	2.00E-05	CC48_SOYBN	CELL DIVISION CYCLE PROTEIN 48 HOMOLOG (VALOSIN CONTAINING PROTEIN HOMOLOG) (VCP)	7.6
743	AF009203	Homo sapiens YAC clone 377A1 unknown mRNA, 3'untranslated region	3.3	<none></none>	<none></none>	<none></none>
744	Z74894	S.cerevisiae chromosome XV reading frame ORF YOL152w	0.12	CD14_RABIT	Q28680 oryctolagus cuniculus (rabbit). monocyte differentiation antigen cd14 precursor. 11/98	1.9
745	U95094	Xenopus laevis XL-INCENP (XL-INCENP) mRNA, complete cds	9.00E-10	KIN3_YEAST	SERINE/THREONI NE-PROTEIN KINASE KIN3 (EC 2.7.1)	2.5
746	U95102	Xenopus laevis mitotic phosphoprotein 90 mRNA, complete cds	2.00E-05	YA53_SCHPO	HYPOTHETICAL 24.2 KD PROTEIN C13A11.03 IN CHROMOSOME I	7.00E-17
747	S61044	ALDH3=aldehyd e dehydrogenase isozyme 3 [human, stomach, mRNA Partial, 1362 nt]	0	DHAP_HUMAN	ALDEHYDE DEHYDROGENAS E, DIMERIC NADP- PREFERRING (EC 1.2.1.5) (CLASS 3)	2.00E-71
748	U95094	Xenopus laevis XL-INCENP (XL-INCENP) mRNA, complete cds	2.00E-08	CA1E_CHICK	COLLAGEN ALPHA 1(XIV) CHAIN PRECURSOR (UNDULIN)	0.36
749	U95102	Xenopus laevis mitotic phosphoprotein 90 mRNA, complete cds	7.00E-06	<none></none>	<none></none>	<none></none>

Table 2

	Nearest Ne	ighbor (BlastN vs. G	Genbank)	Nearest Neighbor (E	BlastX vs. Non-Redund	
SEQ	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
ID						
750	L14815	Entamoeba histolytica HM- 1:IMSS galactose- specific adhesin 170kD subunit (hgl3) gene, complete cds.	0.12	<none></none>	<none></none>	<none></none>
751	X63785	T.thermophila gene for snRNA U2-2	1.1	<none></none>	<none></none>	<none></none>
752	M83756	Mytilus edulis mitochondrial NADH dehydrogenase subunit 5 (ND5) gene, 3' end; NADH dehydrogenase subunit 6 (ND6) gene, complete cds; and cytochrome b (cyt b), 5' end.	0.042	DSC1_HUMAN	DESMOCOLLIN 1A/1B PRECURSOR (DESMOSOMAL GLYCOPROTEIN 2/3) (DG2 / DG3)	2.6
753	AB001066	Brown trout microsatellite DNA sequence	0.38	IMB3_HUMAN	IMPORTIN BETA-3 SUBUNIT (KARYOPHERIN BETA-3 SUBUNIT)	1.2
754	AF064787	Lotus japonicus rac GTPase activating protein 1 mRNA, complete cds	0.51	<none></none>	<none></none>	<none></none>
755	U20608	Dictyostelium discoideum unknown spore germination- specific protein- like protein, orf1, orf2 and orf3 genes, complete cds	0.043	<none></none>	<none></none>	<none></none>
756	M77812	Rabbit myosin heavy chain mRNA, complete cds.	1.2	RBL1_HUMAN	RETINOBLASTOM A-LIKE PROTEIN 1 (107 KD RETINOBLASTOM A-ASSOCIATED PROTEIN) (PRB1) (P107)	4.9

Table 2

		ighbor (BlastN vs. 0	Genbank)		BlastX vs. Non-Redund	
SEQ	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
ID						
757	X63789	T.thermophila genes for snRNA U5-1, snRNA U5- 2	0.058	<none></none>	<none></none>	<none></none>
758	D50646	Mouse mRNA for SDF2, complete cds	2.00E-27	PMT3_YEAST	DOLICHYL- PHOSPHATE- MANNOSE PROTEIN MANNOSYLTRAN SFERASE 3 (EC 2.4.1.109)	0.002
759	L81583	Homo sapiens (subclone 3_g2 from P1 H11) DNA sequence	3.00E-19	ALU5_HUMAN	!!!! ALU SUBFAMILY SC WARNING ENTRY !!!!	0.86
760	U95102	Xenopus laevis mitotic phosphoprotein 90 mRNA, complete cds	2.00E-06	SYFA_YEAST	PHENYLALANYL- TRNA SYNTHETASE ALPHA CHAIN CYTOPLASMIC	5.7
761	AF000370	Homo sapiens polymorphic CA dinucleotide repeat flanking region	6.00E-89	APP1_MOUSE	AMYLOID-LIKE PROTEIN I PRECURSOR (APLP)	5.7
762	U95098	Xenopus laevis mitotic phosphoprotein 44 mRNA, partial cds	0.002	<none></none>	<none></none>	<none></none>
763	U95102	Xenopus laevis mitotic phosphoprotein 90 mRNA, complete cds	7.00E-06	PSF_HUMAN	PTB-ASSOCIATED SPLICING FACTOR (PSF)	0.72
764	AB018288	Homo sapiens mRNA for KIAA0745 protein, partial cds	0	TC2A_CAEBR	TRANSPOSABLE ELEMENT TCB2 TRANSPOSASE	1.5
765	AF020282	Dictyostelium discoideum DG2033 gene, partial cds	0.38	PMT2_YEAST	DOLICHYL- PHOSPHATE- MANNOSE PROTEIN MANNOSYLTRAN SFERASE 2 (EC 2.4.1.109)	0.18

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Table 2

		ighbor (BlastN vs. C	Genbank)		lastX vs. Non-Redund	
1	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
ID						
766	AF017357	Oryza sativa low molecular early light-inducible protein mRNA, complete cds	0.38	RGS3_HUMAN	REGULATOR OF G-PROTEIN SIGNALLING 3 (RGS3) (RGP3)	0.23
767	U67599	Methanococcus jannaschii section 141 of 150 of the complete genome	0.13	<none></none>	<none></none>	<none></none>
768	X74178	B.taurus microsatellite DNA INRA153	0.13	FAG1_SYNY3	P73574 synechocystis sp. (strain pcc 6803). 3- oxoacyl-[acyl-carrier protein] reductase 1 (ec 1.1.1.100) (3- ketoacyl- acyl carrier protein reductase 1). 11/98	5.00E-16
769	AF041858	Mus musculus synaptojanin 2 isoform delta mRNA, partial cds	0.043	CA44_HUMAN	COLLAGEN ALPHA 4(IV) CHAIN PRECURSOR	0.24
770	J01404	Drosophila melanogaster mitochondrial cytochrome c oxidase subunits, ATPase6, 7 tRNAs (Trp, Cys, Tyr, Leu(UUR), Lys, Asp, Gly) genes, and unidentified reading frames A6l, 2 and 3.	0.021	NUIM_CITLA	NADH- UBIQUINONE OXIDOREDUCTAS E CHAIN 1 (EC 1.6.5.3)	7.2
771	AL022317	Human DNA sequence from clone 140L1 on chromosome 22q13.1-13.31, complete sequence [Homo sapiens]	3.00E-41	ALU7_HUMAN	!!!! ALU SUBFAMILY SQ WARNING ENTRY !!!!	4.00E-08
772	U95094	Xenopus laevis XL-INCENP (XL-INCENP) mRNA, complete cds	1.00E-09	<none></none>	<none></none>	<none></none>

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Table 2

ID D	SION DESCRIPTION	CCESSION D				
	1		P VALUE	ACCESSION	DESCRIPTION	P VALUE
773 AF095	protein	pro	Ö	P2C_PARTE	PROTEIN PHOSPHATASE 2C	1.00E-16
	phosphatase 2C mRNA, complete	mF			(EC 3.1.3.16) (PP2C)	
	cds			***		
774 X872	H.sapiens mRNA for cathepsin C		0	CATC_HUMAN	DIPEPTIDYL- PEPTIDASE I	2.00E-46
	•				PRECURSOR (EC 3.4.14.1)	
775 X052	83 Drosophila	X05283 Dr	4.5	<none></none>	<none></none>	<none></none>
773 11032	melanogaster		5	110112	TIONE	1,01,2
	PKCG7 gene					
	exons 7-14 for					
	protein kinase C					
776 X035			0	EF11_HUMAN	ELONGATION	1.00E-83
	for elongation				FACTOR 1-ALPHA	
	factor 1 alpha subunit				1 (EF-1-ALPHA-1)	
777 X069	60 Aspergillus	X06960 As	0.23	<none></none>	<none></none>	<none></none>
	nidulans					
	mitochondrial					
	DNA for					
	cytochrome oxidase subunit 3,					
	tRNA-Tyr					
778 U951	02 Xenopus laevis	U95102 Xe	3.00E-09	YMT8_YEAST	HYPOTHETICAL	5.00E-07
	mitotic				36.4 KD PROTEIN	
	phosphoprotein 90 mRNA,				IN NUP116-FAR3 INTERGENIC	
	complete cds				REGION	
779 U951			2.00E-07	NAT1 YEAST	N-TERMINAL	5.00E-23
	mitotic	mit			ACETYLTRANSFE	
	phosphoprotein				RASE 1 (EC	
	90 mRNA,	l l			2.3.1.88)	
700 11507	complete cds			DDOL CARDE	DOLY (A DD	0.001
780 U597	Of Gallus gallus alternatively		0.014	PPOL_SARPE	POLY (ADP- RIBOSE)	0.021
	spliced AMPA				POLYMERASE (EC	
	glutamate				2.4.2.30) (PARP)	
	receptor, isoform				(` '	į
	GluR2 flop,	Gh				ŀ
	(GluR2) mRNA,					
	partial cds.			370275	21021	- A 103 15
781 U573	P1 Rattus norvegicus FceRI gamma-		1.00E-84	<none></none>	<none></none>	<none></none>
	chain interacting					į
	protein SH2-B					
	(SH2-B) mRNA,	1.				ļ
	complete cds					

Table 2

		ighbor (BlastN vs. (· · · · · · · · · · · · · · · · · · ·	`	BlastX vs. Non-Redund	
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
782		Homo sapiens mRNA for KIAA0691 protein, complete cds	7.00E-57	SSGP_VOLCA	SULFATED SURFACE GLYCOPROTEIN 185 (SSG 185)	5.3
783	AJ008065	Chrysolina bankii 16S rRNA gene, mitotype B2	0.043	<none></none>	<none></none>	<none></none>
784	AF067212	Caenorhabditis elegans cosmid F37F2	0.005	MEKI_RAT	MAPK/ERK KINASE KINASE 1 (EC 2.7.1) (MEK KINASE 1)	4.5
785	U95094	Xenopus laevis XL-INCENP (XL-INCENP) mRNA, complete cds	0.042	<none></none>	<none></none>	<none></none>
786	U95102	Xenopus laevis mitotic phosphoprotein 90 mRNA, complete cds	9.00E-09	<none></none>	<none></none>	<none></none>
787	Y13401	Homo sapiens CD3 delta gene, enhancer sequence	8.00E-08	<none></none>	<none></none>	<none></none>
788	AE001038	Archaeoglobus fulgidus section 69 of 172 of the complete genome	0.13	<none></none>	<none></none>	<none></none>
789	U95102	Xenopus laevis mitotic phosphoprotein 90 mRNA, complete cds	2.00E-06	<none></none>	<none></none>	<none></none>
790	AF041463	Manihot esculenta elongation factor 1-alpha	1.4	<none></none>	<none></none>	<none></none>
791	U95102	Xenopus laevis mitotic phosphoprotein 90 mRNA, complete cds	0.002	HXA3_HAEIN	HEME:HEMOPEXI N-BINDING PROTEIN PRECURSOR	2.7
792	Z12112	pWE15A cosmid vector DNA	3.00E-29	PKWA_THECU	PUTATIVE SERINE/THREONI NE-PROTEIN KINASE PKWA (EC 2.7.1)	2.00E-04

Table 2

		eighbor (BlastN vs. G	Genbank)		BlastX vs. Non-Redund	
	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
ID						
793	U85193	Human nuclear	4.00E-44	<none></none>	<none></none>	<none></none>
		factor I-B2				
		(NFIB2) mRNA,				
704	1100221	complete cds	7.00E-06	NIDI IIIMANI	NEURAL RETINA-	6.3
794	U89331	Human pseudoautosomal	7.00E-00	NRL_HUMAN	SPECIFIC	0.3
		homeodomain-			LEUCINE ZIPPER	
		containing protein			PROTEIN (NRL)	
		(PHOG) mRNA,			, ,	
		complete cds				
795	AF055666	Mus musculus	0.52	PSPD_BOVIN	PULMONARY	0.33
		kinesin light chain			SURFACTANT-	
		2 (Klc2) mRNA,			ASSOCIATED	
		complete cds			PROTEIN D PRECURSOR	
796	L13321	Homo sapiens	0.14	YRP2 YEAST	HYPOTHETICAL	0.27
//	L13321	iduronate-2-	0.14	11d 2_12/101	84.4 KD PROTEIN	0.27
		sulfatase (IDS)			IN RPC2/RET1	
		gene, exon 1,			3'REGION	
		incomplete 5' end.				
797	AL010270	Plasmodium	0.37	YTH3_CAEEL	HYPOTHETICAL 75.5 KD PROTEIN	2
		falciparum DNA ***			C14A4.3 IN	
		SEQUENCING			CHROMOSOME II	
		IN PROGRESS				
		*** from contig				
		4-96, complete				
	*********	sequence	0.015	IN ADOLUMNIA NA	D (DODTE) DETA 2	0.062
798	U95098	Xenopus laevis mitotic	0.015	IMB3_HUMAN	IMPORTIN BETA-3 SUBUNIT	0.063
		phosphoprotein	,		(KARYOPHERIN	
		44 mRNA, partial			BETA-3 SUBUNIT)	
		cds				
799	U70139	Mus musculus	0	CCR4_YEAST	GLUCOSE-	5.00E-11
		putative CCR4			REPRESSIBLE	
		protein mRNA,			ALCOHOL	
		partial cds			DEHYDROGENAS F	
					TRANSCRIPTIONA	
					L EFFECTOR	
					(CARBON	
					CATABOLITE	
					REPRESSOR	
900	1.06507	Managarate	2.000 41	MNIE MOUGE	PROTEIN 4)	4.00E-18
800	L26507	Mouse myocyte nuclear factor	3.00E-41	MNF_MOUSE	MYOCYTE NUCLEAR	4.UUE-18
		(MNF) mRNA,			FACTOR (MNF)	
		complete cds.				
		1		l	.1	

Table 2

		ghbor (BlastN vs. 6			r (BlastX vs. Non-Redundar	
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
801	U20527	Mus musculus chemokine KC gene, 5' region.	0	GRO_MOUSE	GROWTH REGULATED PROTEIN PRECURSOR (PLATELET-DERIVED GROWTH FACTOR- INDUCIBLE PROTEIN KC) (SECRETORY PROTEIN N51)	1.00E-28
802	AF065482	Homo sapiens sorting nexin 2 (SNX2) mRNA, complete cds	0	_	MYOSIN HEAVY CHAIN, MUSCLE	0.089
803	U05823	Mus musculus pericentrin mRNA, complete cds.	1.00E-94	M84D_DROME	MALE SPECIFIC SPERM PROTEIN MST84DD	0.099
804	U67468	Methanococcus jannaschii section 10 of 150 of the complete genome	0.4	<none></none>	<none></none>	<none></none>
805	U14178	Human type II IL-1 receptor gene, exon 1B	1.00E-19	AMPH_HUMAN	AMPHIPHYSIN	2.9
806	L40411	Homo sapiens thyroid receptor interactor	0	TR18_HUMAN	THYROID RECEPTOR INTERACTING PROTEIN 8 (TRIP8)	4.00E-86
807	D17218	Human HepG2 3' region Mbol cDNA, clone hmd3g02m3	e-136	CA1A_HUMAN	COLLAGEN ALPHA 1(X) CHAIN PRECURSOR	3.00E-04
808	Z57610	H.sapiens CpG DNA, clone 187a10, reverse read cpg187a10.rt1a.	e-102	HN3B_MOUSE	HEPATOCYTE NUCLEAR FACTOR 3- BETA (HNF-3B)	1.00E-24
809	D14678	Human mRNA for kinesin- related protein, partial cds	0	NCD_DROME	CLARET SEGREGATIONAL PROTEIN	1.00E-70

Table 2

		ghbor (BlastN vs. 6		Nearest Neighbo	or (BlastX vs. Non-Redundar	nt Proteins)
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
810	X56317	Xiphophorus maculatus Xmrk(proto- oncogene) gene for receptor tyrosine kinase.	0.49	WN1B_MOUSE	WNT-10B PROTEIN PRECURSOR (WNT-12)	7.2
811	M36200	Human synaptobrevin 1 (SYB1) gene, exon 5.	0.2	VE2_HPV14	REGULATORY PROTEIN E2	3.1
812	M18157	Human glandular kallikrein gene, complete cds.	1.5	EKLF_MOUSE	ERYTHROID KRUEPPEL-LIKE TRANSCRIPTION FACTOR (EKLF)	1.1
813	D25215	Human mRNA for KIAA0032 gene, complete cds	1.9	YXIS_SACER	HYPOTHETICAL 28.9 KD PROTEIN IN XIS 5'REGION (ORF1)	1.3
814	M96628	Human gene sequence, 5' end.	2.00E-06	AGRI_DISOM	AGRIN (FRAGMENT)	9.5
815	Z57610	H.sapiens CpG DNA, clone 187a10, reverse read cpg187a10.rt1a.	e-102	HN3B_MOUSE	HEPATOCYTE NUCLEAR FACTOR 3- BETA (HNF-3B)	1.00E-19
816	X14168	Human pLC46 with DNA replication origin	5.00E-16	ZN44_HUMAN	ZINC FINGER PROTEIN 44 (ZINC FINGER PROTEIN KOX7)	1.6
817	M19262	Rat clathrin light chain (LCB3) mRNA, complete cds.	0.28	LMA_DROME	LAMININ ALPHA CHAIN PRECURSOR	4.7
818	AF058055	Mus musculus monocarboxylate transporter 1	0.2	<none></none>	<none></none>	<none></none>
819	AB014570	Homo sapiens mRNA for KIAA0670 protein, partial cds	0.16	YGR1_YEAST	HYPOTHETICAL 34.8 KD PROTEIN IN SUT1- RCK1 INTERGENIC REGION	4.00E-06
820	M19262	Rat clathrin light chain (LCB3) mRNA, complete cds.	0.27	LMA_DROME	LAMININ ALPHA CHAIN PRECURSOR	4.5

Table 2

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non-Redundant Proteins)				
SEQ	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE		
ID						_		
821	Z54367	H.sapiens gene for plectin	0.29	YO93_CAEEL	HYPOTHETICAL 58.5 KD PROTEIN T20B12.3 IN CHROMOSOME III	1.00E-14		
822	AB017026	Mus musculus mRNA for oxysterol- binding protein, complete cds	0	OXYB_HUMAN	OXYSTEROL-BINDING PROTEIN	2.00E-49		
823	X58170	M.musculus mRNA for t- Complex Tcp- 10a gene	1.00E-20	UL52_HSV11	DNA HELICASE/PRIMASE COMPLEX PROTEIN (DNA REPLICATION PROTEIN UL52)	5.3		
824	X58430	Human Hox1.8 gene	0	HXAA_HUMAN	HOMEOBOX PROTEIN HOX-A10 (HOX-1H) (HOX-1.8) (PL)	1.00E-44		
825	X53754	Porcine sarcoplasmic/end oplasmic- reticulum Ca(2+) pump gene 2 3'- end region	1.3	<none></none>	<none></none>	<none></none>		
826	AB005786	Arabidopsis thaliana tRNA- Glu gene	0.46	<none></none>	<none></none>	<none></none>		
827	AB012130	Homo sapiens SBC2 mRNA for sodium bicarbonate cotransporter2, complete cds	1.9	<none></none>	<none></none>	<none></none>		
828	AB017430	Homo sapiens mRNA for kinesin-like DNA binding protein, complete cds	0	YBAV_ECOLI	HYPOTHETICAL 12.7 KD PROTEIN IN HUPB- COF INTERGENIC REGION	0.063		
829	AB007886	Homo sapiens KIAA0426 mRNA, complete cds	0.042	YDF3_SCHPO	PROBABLE EUKARYOTIC INITIATION FACTOR C17C9.03	0.52		
830	AB018335	Homo sapiens mRNA for KIAA0792 protein, complete cds	e-172	UROT_BOVIN	TISSUE PLASMINOGEN ACTIVATOR PRECURSOR (EC 3.4.21.68)	0.86		

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Table 2

	•	ghbor (BlastN vs. 0	Genbank)	Nearest Neighbor (BlastX vs. Non-Redundant Proteins) ACCESSION DESCRIPTION P VALUE			
SEQ	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	CESSION DESCRIPTION		
ID							
831	D12646	Mouse kif4 mRNA for microtubule- based motor protein KIF4, complete cds	0	KIF4_MOUSE	KINESIN-LIKE PROTEIN KIF4	9.00E-96	
832	U38376	Rattus norvegicus cytosolic phospholipase A2 mRNA, complete cds	0.048	<none></none>	<none></none>	<none></none>	
833	L40411	Homo sapiens thyroid receptor interactor	0	TRI8_HUMAN	THYROID RECEPTOR INTERACTING PROTEIN 8 (TRIP8)	4.00E-86	
834	U08110	Mus musculus RNA1 homolog (Fug1) mRNA, complete cds.	8.00E-04	YNW7_YEAST	HYPOTHETICAL 68.8 KD PROTEIN IN URE2- SSU72 INTERGENIC REGION	0.02	
835	D50646	Mouse mRNA for SDF2, complete cds	1.00E-40	YB64_YEAST	HYPOTHETICAL 57.2 KD PROTEIN IN MET8- HPC2 INTERGENIC REGION	4.9	
836	D50646	Mouse mRNA for SDF2, complete cds	1.00E-40	YB64_YEAST	HYPOTHETICAL 57.2 KD PROTEIN IN MET8- HPC2 INTERGENIC REGION	4.9	
837	U67459	Methanococcus jannaschii section 1 of 150 of the complete genome	5.00E-05	GCS1_HUMAN	MANNOSYL- OLIGOSACCHARIDE GLUCOSIDASE (EC 3.2.1.106)	9.2	
838	U18657	Haemophilus influenzae LeuA (leuA) gene, partial cds, DprA (dprA+), orf272 and orf193 genes, complete cds, and PfkA (pfkA) gene, partial cds.	0.01	STE6_YEAST	MATING FACTOR A SECRETION PROTEIN STE6 (MULTIPLE DRUG RESISTANCE PROTEIN HOMOLOG) (P-GLYCOPROTEIN)	7	

Table 2

	Nearest Neig	ghbor (BlastN vs.	Genbank)	Nearest Neighbor (BlastX vs. Non-Redundant Proteins)				
SEQ	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE		
ID								
839	U12523	Rattus norvegicus ultraviolet B radiation- activated UV98 mRNA, partial sequence.	1.00E-10	YMT8_YEAST	HYPOTHETICAL 36.4 KD PROTEIN IN NUP116-FAR3 INTERGENIC REGION	2.00E-06		
840	D78255	Mouse mRNA for PAP-1, complete cds	e-175	<none></none>	<none></none>	<none></none>		
841	D17263	Human HepG2 3' region MboI cDNA, clone hmd5f07m3	1.00E-58	<none></none>	<none></none>	<none></none>		
842	AF006751	Homo sapiens ES/130 mRNA, complete cds	0.061	YRP2_YEAST	HYPOTHETICAL 84.4 KD PROTEIN IN RPC2/RET1 3'REGION	2.00E-07		
843	U67459	Methanococcus jannaschii section 1 of 150 of the complete genome	6.00E-05	YC14_METJA	HYPOTHETICAL PROTEIN MJ1214	8.1		
844	D88689	Mus musculus mRNA for flt-1, complete cds	0.084	ICP0_HSV2H	TRANS-ACTING TRANSCRIPTIONAL PROTEIN ICP0 (VMW118 PROTEIN)	0.014		

Table 5 All Differential Data for Libs 1-4 and 8-9

Clone Name	Cluster ID	Clones in Lib1	Clones in Lib2	Clones in Lib3	Clones in Lib4	Clones in Lib8	Clones in Lib9
M00001340B:A06	17062	3	0	0	0	0	0
M00001340D:F10	11589	2	2	1	3	3	8
M00001341A:E12	4443	10	6	2	6	3	11
M00001342B:E06	39805	2	0	0	0	1	0
M00001343C:F10	2790	7	15	13	14	6	0
M00001343D:H07	23255	3	0	1	1	0	0
M00001345A:E01	6420	8	0	2	0	1	0
M00001346A:F09	5007	4	8	3	6	2	6
M00001346D:E03	6806	5	2	1	2	0	3
M00001346D:G06	5779	5	4	3	4	0	0
M00001346D:G06	5779	5	4	3	4	0	0
M00001340B:B00	13576	5	0	0	0	12	11
M0000134771:B10	16927	4	0	0	2	0	0
M00001348B:G06	16985	4	0	0	0	0	0
M00001349B:B08	3584	5	11	5	0	0	2
M00001349B:B00	7187	5	3	1	0	- 1	0
M00001350A:1101 M00001351B:A08	3162	10	14	1	6	6	5
M00001351B:A08	3162	10	14	1	6	6	5
M00001351B:A00	16245	4	0	0	0	0	0
M00001352A:E02	8078	4	3	1	0	1	0
M00001353A:G12	14929	4	0	0	1	23	16
M00001355B:G10	14391	3	1	0	0	0	0
M00001353B:G10	4059	8	6	8	16	0	1
M00001337D:D11	4141	5	2	10	16	4	27
M00001361D:F08	2379	26	13	4	2	2	3
M00001361D.F08	5622	7	4	2	13	1	2
M00001362B:D10	945	9	21	2	13	0	0
M00001365C:C10	40132	2	0	0	0	3	0
M00001303C.C10	6867	7	3	0	0	0	0
M00001370A.C09	7172	3	5	1	2	0	1
M00001371C.E09	17732	1	3	5	0	1	4
M00001378B:B02	39833	2	0	0	0	0	0
M00001378B:B02	1334	27 27	38	35	28	3	0
		2	0	0	0	0	0
M00001380D:B09 M00001382C:A02	39886 22979	2	1	0	0	0	0
	39648	2	0	0	0	0	0
M00001383A:C03	39648	2	0	0	0	0	0
M00001383A:C03		5	5	4	2	5	2
M00001386C:B12	5178			25	16	1	0
M00001387A:C05	2464	5	19		0	0	0
M00001387B:G03	7587 5033	6	2	1		5	0
M00001388D:G05	5832	10	3	0	1		
M00001389A:C08	16269	3	0	0	0	1	1
M00001394A:F01	6583	2	7	3	2	0	0
M00001395A:C03	4016	5	14	0	6	0	0
M00001396A:C03	4009	6	4	13	5	4	10
M00001402A:E08	39563	2	0	0	0	0	0

Table 5 All Differential Data for Libs 1-4 and 8-9

Clone Name	ID	Clones in Lib1	Clones in Lib2	Clones in Lib3	Clones in Lib4	Clones in Lib8	Clones in Lib9
M00001407B:D11	5556	8	1	5	0	2	0
M00001409C:D12	9577	5	2	0	1	11	12
M00001410A:D07	7005	8	2	0	0	0	0
M00001412B:B10	8551	4	4	0	3	0	0
M00001415A:H06	13538	5	0	0	0	9	1
M00001416A:H01	7674	5	2	0	5	0	0
M00001416B:H11	8847	4	1	3	0	6	1
M00001417A:E02	36393	2	0	0	1	0	0
M00001418B:F03	9952	4	2	1	1	0	0
M00001418D:B06	8526	3	2	1	5	1	0
M00001421C:F01	9577	5	2	0	1	11	12
M00001423B:E07	15066	4	0	0	0	0	0
M00001424B:G09	10470	5	1	0	2	0	1
M00001425B:H08	22195	3	0	0	0	0	0
M00001426D:C08	4261	4	9	7	9	12	15
M00001428A:H10	84182	1	0	0	0	0	0
M00001429A:H04	2797	15	11	18	16	1	14
M00001429B:A11	4635	7	9	2	0	0	0
M00001429D:D07	40392	2	0	1	8	12	16
M00001439C:F08	40054	1	0	0	0	0	0
M00001442C:D07	16731	3	1	0	0	0	0
M00001445A:F05	13532	3	2	1	0	1	2
M00001446A:F05	7801	5	2	4	6	.1	0
M00001447A:G03	10717	7	2	0	5	8	0
M00001448D:C09	8	1850	2127	1703	3133	1355	122
M00001448D:H01	36313	2	0	0	0	1	30
M00001449A:A12	5857	6	2	3	4	0	0
M00001449A:B12	41633	1	1	0	0	0	0
M00001449A:D12	3681	12	5	10	1	2	5
M00001449A:G10	36535	2	0	0	0	0	0
M00001449C:D06	86110	1	0	0	0	0	0
M00001450A:A02	39304	2	0	0	0	0	0
M00001450A:A11	32663	1	1	0	0	0	0
M00001450A:B12	82498	1	0	0	0	0	0
M00001450A:D08	27250	2	0	0	0	0	0
M00001452A:B04	84328	1	0	0	0	0	0
M00001452A:B12	86859	1	0	0	0	0	0
M00001452A:D08	1120	44	41	5	1 1	5	0
M00001452A:F05	85064	1	0	0	0	0	0
M00001452C:B06	16970	4	0	0	0	3	4
M00001453A:E11	16130	3	1	0	0	0	1
M00001453C:F06	16653	3	1	0	0	0	0
M00001453C:100	83103	1	0	0	0	0	0
M00001454R:C12	7005	8	2	0	0	0	0
M00001454D:G03	689	58	95	17	36	66	95
M00001454D:G05	13238	4	1	0	0	0	0
M00001455A:E09	13072	4	1	0	0	0	0
M00001455D:F09	9283	4	1	0	1	0	1
141000001433D*1.03	9403	-	1	J	1	0	1

Table 5 All Differential Data for Libs 1-4 and 8-9

Clone Name	Cluster ID	Clones in Lib1	Clones in Lib2	Clones in Lib3	Clones in Lib4	Clones in Lib8	Clones in Lib9
M00001455D:F09	9283	4	1	0	1	0	1
M00001460A:F06	2448	23	22	2	3	3	1
M00001460A:F12	39498	2	0	0	0	0	0
M00001461A:D06	1531	20	23	32	17	14	14
M00001463C:B11	19	1415	1203	1364	525	479	774
M00001465A:B11	10145	2	0	2	0	0	0
M00001466A;E07	4275	11	2	5	0	4	2
M00001467A:B07	38759	2	0	0	0	1	1
M00001467A:D04	39508	2	0	0	0	0	0
M00001467A:D08	16283	3	0	0	0	0	0
M00001467A:D08	16283	3	0	0	0	0	0
M00001467A:E10	39442	2	0	0	0	0	0
M00001468A:F05	7589	6	2	1	1	1	0
M00001469A:C10	12081	4	0	0	0	0	0
M00001469A:H12	19105	2	0	2	0	1	0
M00001470A:B10	1037	53	48	4	22	0	0
M00001470A:C04	39425	2	0	0	0	0	0
M00001471A:B01	39478	2	0	0	0	0	0
M00001481D:A05	798 5	3	1	4	0	1	0
M00001490B:C04	18699	2	1	0	0	0	3
M00001494D:F06	7206	4	3	3	1	2	0
M00001497A:G02	2623	12	4	31	4	6	1
M00001499B:A11	10539	2	1	1	0	1	0
M00001500A:C05	5336	9	2	4	8	3	15
M00001500A:E11	2623	12	4	31	4	6	1
M00001500C:E04	9443	4	2	1	1	0	0
M00001501D:C02	9685	3	2	0	7	2	3
M00001504C:A07	10185	5	1	0	0	2	4
M00001504C:H06	6974	7	3	0	1	0	0
M00001504D:G06	6420	8	0	2	0	1	0
M00001507A:H05	39168	2	0	0	0	0	0
M00001511A:H06	39412	2	0	0	0	0	0
M00001512A:A09	39186	2	0	0	0	0	0
M00001512D:G09	3956	9	9	5	2	0	0
M00001513A:B06	4568	10	4	0	9	2	0
M00001513C:E08	14364	1	0	0	0	0	0
M00001514C:D11	40044	2	0	0	0	0	0
M00001517A:B07	4313	13	6	1	0	1	0
M00001518C:B11	8952	3	4	0	4	2	0
M00001528A:C04	7337	4	4	3	16	12	21
M00001528A:F09	18957	3	0	0	0	0	0
M00001528B:H04	8358	3	3	2	0	0	0
M00001531A:D01	38085	2	0	0	0	0	0
M00001532B:A06	3990	6	12	4	1	3	1
M00001533A:C11	2428	14	14	13	9	2	19
M00001534A:C04	16921	4	0	0	1	2	1
M00001534A:D09	5097	6	5	1	1	3	2
M00001534A:F09	5321	11	7	1	5	10	26

Table 5 All Differential Data for Libs 1-4 and 8-9

Clone Name	Cluster ID	Clones in Lib1	Clones in Lib2	Clones in Lib3	Clones in Lib4	Clones in Lib8	Clones in Lib9
M00001534C:A01	4119	9	4	2	2	5	3
M00001535A:B01	7665	3	1	5	0	0	0
M00001535A:C06	20212	2	0	1	1	0	0
M00001535A:F10	39423	2	0	0	0	0	0
M00001536A:B07	2696	23	11	9	18	10	21
M00001536A:C08	39392	2	0	0	0	0	0
M00001537A:F12	39420	2	0	0	0	0	0
M00001537B:G07	3389	4	11	13	2	0	0
M00001540A:D06	8286	6	1	0	3	4	0
M00001541A:D02	3765	19	6	0	0	0	0
M00001541A:F07	22085	3	0	0	0	0	1
M00001541A:H03	39174	2	0	0	0	0	0
M00001542A:A09	22113	3	0	0	0	0	0
M00001542A:E06	39453	2	0	0	0	0	0
M00001544A:E03	12170	2	1	2	0	0	0
M00001544A:G02	19829	2	0	1	0	0	0
M00001544B:B07	6974	7	3	0	1	0	0
M00001545A:C03	19255	2	0	0	0	0	0
M00001545A:D08	13864	3	0	2	1	2	4
M00001546A:G11	1267	43	55	5	0	0	0
M00001548A:E10	5892	5	1	4	4	1	3
M00001548A:H09	1058	40	44	37	47	39	59
M00001549A:B02	4015	10	5	8	15	2	0
M00001549A:D08	10944	3	0	3	1	0	7
M00001549B:F06	4193	12	7	2	2	0	1
M00001549C:E06	16347	4	0	0	0	0	0
M00001550A:A03	7239	5	2	1	0	2	0
M00001550A:G01	5175	8	1	3	2	0	0
M00001551A:B10	6268	6	4	3	18	5	0
M00001551A:F05	39180	2	0	0	0	0	0
M00001551A:G06	22390	2	1	0	0	0	1
M00001551C:G09	3266	12	14	0	1	0	6
M000015516:B09	307	73	60	196	75	79	27
M00001552A:D11	39458	2	0	0	0	0	0
M00001552B:D04	5708	5	4	4	3	1	4
M00001552B:D04	8298	4	3	1	3	0	0
M00001553B:F12	4573	5	7	2	5	0	1
M00001553B:112	22814	3	0	0	0	0	0
M00001555A:B02	39539	2	0	0	0	1	0
M00001555A:B02	39195	2	0	0	0	0	0
M00001555A:C01	39193 4561	8	4	4	8	0	0
M00001555D:G10		2	0	3	2	10	17
M00001556A:C09	9244				3	4	0
	1577	12	40	25			
M00001556A:H01	15855	2	1	1	2	12	213
M00001556B:C08	4386	7	8	3	1	3	21
M00001556B:G02	11294	4	0	2	0	0	1
M00001557A:D02	7065	5	3	2	1	0	0
M00001557A:D02	7065	5	3	2	1	0	0

Table 5 All Differential Data for Libs 1-4 and 8-9

Clone Name	Cluster ID	Clones in Lib1	Clones in Lib2	Clones in Lib3	Clones in Lib4	Clones in Lib8	Clones in Lib9
M00001557A:F01	9635	3	0	2	1	0	0
M00001557A:F03	39490	2	0	0	0	1	0
M00001557B:H10	5192	8	5	0	5	0	0
M00001557D:D09	8761	3	4	0	1	0	l
M00001558B:H11	7514	5	3	0	0	0	0
M00001560D:F10	6558	4	3	4	0	0	5
M00001561A:C05	39486	2	0	0	0	0	0
M00001563B:F06	102	289	233	278	116	123	184
M00001564A:B12	5053	11	4	2	2	1	1
M00001571C:H06	5749	4	1	9	0	0	0
M00001578B:E04	23001	2	1	0	2	0	0
M00001579D:C03	6539	8	3	0	0	0	1
M00001583D:A10	6293	3	5	2	6	0	0
M00001586C:C05	4623	3	4	12	2	1	1
M00001587A:B11	39380	2	0	0	0	0	0
M00001594B:H04	260	189	188	27	2	15	0
M00001597C:H02	4837	6	2	10	0	3	1
M00001597D:C05	10470	5	1	0	2	0	1
M00001598A:G03	16999	4	0	0	0	0	0
M00001601A:D08	22794	2	0	0	0	0	0
M00001604A:B10	1399	49	27	19	7	10	23
M00001604A:F05	39391	2	0	0	0	0	0
M00001607A:E11	11465	5	0	0	0	0	0
M00001608A:B03	7802	5	4	0	1	0	0
M00001608B:E03	22155	3	0	0	0	0	0
M00001606B:E05	13157	4	1	0	3	1	0
M00001617C:E02	17004	4	0	1	0	1	0
M00001617C:E02	40314	2	Ö	0	0	1	0
M00001617C:112	40044	2	Ö	0	0	0	0
M00001623D:F10	13913	2	1	2	0	0	1
M00001624A:B06	3277	10	11	8	3	5	1
M00001624C:F01	4309	4	13	3	10	0	0
M00001624C:101	5214	10	2	2	2	4	3
M00001636B:1103	39171	2	0	0	0	0	0
M00001645A:C12	19267	2	0	0	0	0	1
M00001648C:A01	4665	5	9	0	0	0	0
M00001648C.A01 M00001657D:C03	23201	3	0	0	0	3	0
M00001657D:C03	76760	1	0	2	2	0	5
M00001657D.F08	23218	3	0	0	0	0	0
		2	0	0	0	0	0
M00001663A:E04	35702		-		8		0
M00001669B:F02	6468	4	3	3	0	1	0
M00001670C:H02	14367	3	0	0		0	
M00001673C:H02	7015	6	3	1	2	1	1
M00001675A:C09	8773	4	1	4	4	4	6
M00001676B:F05	114.60	4	2	0	0	0	0
M00001677C:E10	14627	1	2	1	0	1	0
M00001677D:A07	7570	5	3	0	0	0	0
M00001678D:F12	4416	9	5	2	6	1	3

Table 5 All Differential Data for Libs 1-4 and 8-9

Clone Name	Cluster ID	Clones in Lib1	Clones in Lib2	Clones in Lib3	Clones in Lib4	Clones in Lib8	Clones in Lib9
M00001679A:A06	6660	7	0	4	2	1	0
M00001679A:F10	26875	1	0	0	0	1	0
M00001679B:F01	6298	2	4	5	3	1	0
M00001679C:F01	78091	1	0	0	0	0	0
M00001679D:D03	10751	3	2	0	1	0	1
M00001679D:D03	10751	3	2	0	1	0	1
M00001680D:F08	10539	2	1	1	0	1	0
M00001682C:B12	17055	4	0	0	0	0	0
M00001686A:E06	4622	7	6	4	2	3	0
M00001688C:F09	5382	6	2	6	2	0	3
M00001693C:G01	4393	10	6	2	4	1	1
M00001716D:H05	67252	1	0	0	1	0	0
M00003741D:C09	40108	2	0	0	0	0	0
M00003747D:C05	11476	6	0	0	0	0	0
M00003759B:B09	697	76	52	30	72	21	30
M00003762C:B08	17076	4	0	0	0	0	0
M00003763A:F06	3108	14	11	7	5	0	1
M00003774C:A03	67907	1	0	0	0	0	0
M00003796C:D05	5619	3	5	3	3	0	4
M00003826B:A06	11350	3	3	0	0	1	0
M00003833A:E05	21877	2	1	0	0	0	1
M00003837D:A01	7899	5	4	0	2	1	0
M00003839A:D08	7798	5	2	2	0	0	1
M00003844C:B11	6539	8	3	0	0	0	1
M00003846B:D06	6874	6	3	0	0	0	0
M00003851B:D10	13595	4	0	1	0	0	1
M00003853A:D04	5619	3	5	3	3	. 0	4
M00003853A:F12	10515	5	1	0	1	1	2
M00003856B:C02	4622	7	6	4	2	3	0
M00003857A:G10	3389	4	11	13	2	0	0
M00003857A:H03	4718	4	5	5	2	4	6
M00003871C:E02	4573	5	7	2	5	0	1
M00003875B:F04	12977	5	Ó	0	0	0	0
M00003875B:F04	12977	5	0	0	0	0	0
M00003875C:G07	8479	4	3	1	1	2	4
M00003875C:G07	7798	5	2	2	0	0	1
M00003870B:C11	5345	7	1	7	4		27
M00003879B:D10	31587	1	1	0	0	6 1	
M00003879B:D10	14507	3	1			3	0
M00003879D:A02				0	0		1
M00003885C:A02	13576	5	0	0	0	12	11
	13576	5	0	0	0	12	11
M00003906C:E10	9285	4	3	0	0	1	2
M00003907D:A09	39809	1	0	0	0	2	1
M00003907D:H04	16317	3	0	0	0	0	0
M00003909D:C03	8672	4	4	0	0	0	0
M00003912B:D01	12532	4	1	0	1	0	1
M00003914C:F05	3900	9	6	8	1	7	13
M00003922A:E06	23255	3	0	1	1	0	0

Table 5 All Differential Data for Libs 1-4 and 8-9

Clone Name	Cluster ID	Clones in Lib1	Clones in Lib2	Clones in Lib3	Clones in Lib4	Clones in Lib8	Clones in Lib9
M00003958A:H02	18957	3	0	0	0	0	0
M00003958A:H02	18957	3	0	0	0	0	0
M00003958C:G10	40455	2	0	0	0	0	0
M00003958C:G10	40455	2	0	0	0	0	0
M00003968B:F06	24488	2	0	1	4	0	0
M00003970C:B09	40122	2	0	0	0	0	0
M00003974D:E07	23210	3	0	0	0	0	0
M00003974D:H02	23358	3	0	0	0	1	0
M00003975A:G11	12439	4	0	0	0	0	0
M00003978B:G05	5693	7	4	1	3	1	1
M00003981A:E10	3430	9	10	7	3	0	0
M00003982C:C02	2433	10	13	21	18	8	8
M00003983A:A05	9105	5	1	1	1	0	0
M00004028D:A06	6124	4	8	1	9	1	0
M00004028D:C05	40073	2	0	1	0	0	1
M00004031A:A12	9061	5	2	0	0	0	0
M00004031A:A12	9061	5	2	0	0	0	0
M00004035C:A07	37285	2	0	0	1	0	1
M00004035D:B06	17036	4	0	0	0	0	0
M00004059A:D06	5417	10	4	0	9	2	0
M00004068B:A01	3706	7	14	4	22	1	0
M00004072B:B05	17036	4	0	0	0	0	0
M00004081C:D10	15069	3	0	0	1	0	0
M00004081C:D12	14391	3	1	0	0	0	0
M00004086D:G06	9285	4	3	0	0	1	2
M00004087D:A01	6880	2	6	1	1	0	0
M00004093D:B12	5325	5	5	2	0	2	1
M00004093D:B12	5325	5	5	2	0	2	i
M00004105C:A04	7221	5	2	2	2	0	0
M00004108A:E06	4937	4	9	3	1	3	1
M00004111D:A08	6874	6	3	0	0	0	0
M00004114C:F11	13183	2	3	0	7	0	1
M00004138B:H02	13272	3	2	0	3	0	0
M00004146C:C11	5257	2	8	5	5	5	25
M00004151D:B08	16977	4	0	0	0	0	0
M00004157C:A09	6455	3	1	6	0	0	0
M00004169C:C12	5319	6	2	8	2	2	3
M00004171D:B03	4908	6	7	2	2	2	0
M00004172C:D08	11494	4	Ó	0	0	0	0
M00004183C:D07	16392	3	0	0	0	0	0
M00004185C:C03	11443	5	1	0	0	0	0
M00004197D:H01	8210	2	6	0	0	0	0
M00004197B:1101	14311	4	0	0	0		
M00004203B:C12 M00004212B:C07	2379	26	13	4	2	1	2
M00004212B:C07	11451	3	2		2	2	3
M00004214C:H03	16918	<i>3</i> 4	0	1 0		1	1
M00004223A:G10	7899				0	0	0
M00004223B:D09	12971	5 4	4	0	2	1	0
171000007223D.E04	147/1	4	0	0	0	1	0

Table 5 All Differential Data for Libs 1-4 and 8-9

	Clone Name	Cluster	Clones in	Clones in	Clones in	Clones in	Clones in	Clones in
		ID	Lib1	Lib2	Lib3	Lib4	Lib8	Lib9
M	100004229B:F08	6455	3	1	6	0	0	0
M	I00004230B:C07	7212	3	5	2	1	3	0
M	00004269D:D06	4905	7	6	3	1	3	1
M	[00004275C:C11	16914	3	0	0	1	0	0
M	000042 8 3B:A04	14286	3	1	0	1	1	1
M	I00004285B:E08	56020	1	0	0	0	0	0
M	100004295D:F12	16921	4	0	0	1	2	1
M	00004296C:H07	13046	4	1	0	1	0	0
M	00004307C:A06	9457	2	0	5	0	3	0
M	00004312A:G03	26295	2	0	0	0	0	0
M	00004318C:D10	21847	2	1	0	0	0	0
M	00004372A:A03	2030	13	10	32	4	0	0
M	100004377C:F05	2102	12	20	23	21	6	5

Table 6 All Differential Data for Libs 15-20

Clone Name	Cluster ID	Clones in Lib15	Clones in Lib16b	Clones in Lib17	Clones in Lib18	Clones in Lib19	Clones in Lib20
M00001340B:A06	17062	0	0	0	0	0	0
M00001340D:F10	11589	0	0	0	0	0	0
M00001341A:E12	4443	0	0	0	1	0	0
M00001342B:E06	39805	0	0	0	0	0	0
M00001343C:F10	2790	0	0	0	0	0	0
M00001343D:H07	23255	0	0	0	0	0	0
M00001345A:E01	6420	0	0	0	0	0	0
M00001346A:F09	5007	0	0	0	0	0	0
M00001346D:E03	6806	0	0	0	0	0	0
M00001346D:G06	5779	0	0	0	0	0	0
M00001346D:G06	5779	0	0	0	0	0	0
M00001347A:B10	13576	0	0	0	0	0	0
M00001348B:B04	16927	0	0	0	0	0	0
M00001348B:G06	16985	0	0	0	0	0	0
M00001349B:B08	3584	0	0	0	0	0	0
M00001350A:H01	7187	0	0	0	0	0	0
M00001351B:A08	3162	0	1	0	0	1	0
M00001351B:A08	3162	0	1	0	0	1	0
M00001352A:E02	16245	0	0	0	0	0	0
M00001353A:G12	8078	0	0	0	0	0	0
M00001353D:D10	14929	0	3	1	0	5	0
M00001355B:G10	14391	0	0	0	0	0	0
M00001357D:D11	4059	0	0	0	0	0	0
M00001361A:A05	4141	0	0	0	0	0	0
M00001361D:F08	2379	0	0	0	0	0	0
M00001362B:D10	5622	0	0	0	0	0	0
M00001362C:H11	945	0	0	0	0	0	1
M00001365C:C10	40132	0	0	0	0	0	0
M00001370A:C09	6867	0	0	0	0	0	0
M00001371C:E09	7172	0	0	0	0	0	0
M00001376B:G06	17732	0	0	0	0	0	1
M00001378B:B02	39833	0	0	0	0	0	0
M00001379A:A05	1334	0	0	0	0	0	1
M00001380D:B09	39886	0	0	0	0	0	0
M00001382C:A02	22979	0	0	0	0	0	0
M00001383A:C03	39648	0	0	0	0	0	0
M00001383A:C03	39648	0	0	0	0	0	0
M00001386C:B12	5178	0	0	0	0	0	0
M00001387A:C05	2464	0	0	0	0	0	0
M00001387B:G03	7587	0	0	0	0	0	0
M00001388D:G05	5832	0	0	0	0	0	0
M00001389A:C08	16269	0	1	0	0	0	0
M00001394A:F01	6583	1	4	1	0	0	0
M00001395A:C03	4016	0	0	0	0	0	0
M00001396A:C03	4009	0	0	0	0	0	0
M00001402A:E08	39563	0	0	0	0	0	0
M00001407B:D11	5556	0	0	0	0	0	0
M00001409C:D12	9577	0	0	0	0	0	0

Table 6 All Differential Data for Libs 15-20

Table 6 All Differential Data for Libs 15-20							
Clone Name	Cluster ID	Clones in Lib15	Clones in Lib16b	Clones in Lib17	Clones in Lib18	Clones in Lib19	Clones in Lib20
M00001410A:D07	7005	0	0	0	0	0	0
M00001410A:D07	8551	0	0	0	0	0	0
M00001412B.B10 M00001415A:H06	13538	0	0	0	0	0	0
M00001415A:1100 M00001416A:H01	7674	0	0	0	0	0	0
M00001416A:H01	8847	0	0	0	0	0	0
M00001410B.H11	36393	0	0	0	0	0	0
M00001417A.E02 M00001418B:F03	9952	0	0	0	0	0	0
M00001418D:B06	8526	0	0	0	0	0	0
	9577	0	0	0	0	0	0
M00001421C:F01	15066	0	0	0	0	0	0
M00001423B:E07		_	0	0	0	0	0
M00001424B:G09	10470	0	-		0	0	0
M00001425B:H08	22195	0	0	0		0	1
M00001426D:C08	4261	0	0	1	0	<u>-</u>	0
M00001428A:H10	84182	0	0	0	0	0	
M00001429A:H04	2797	0	0	0	0	0	0
M00001429B:A11	4635	0	0	0	0	0	0
M00001429D:D07	40392	0	0	0	0	0	0
M00001439C:F08	40054	0	0	0	0	0	0
M00001442C:D07	16731	0	0	0	0	0	0
M00001445A:F05	13532	0	0	0	0	0	0
M00001446A:F05	7801	0	0	0	0	0	0
M00001447A:G03	10717	0	0	0	0	0	0
M00001448D:C09	8	1	6	6	1	14	1
M00001448D:H01	36313	0	3	0	0	3	0
M00001449A:A12	5857	0	0	0	0	0	0
M00001449A:B12	41633	0	0	0	0	0	0
M00001449A:D12	3681	0	0	0	0	0	0
M00001449A:G10	36535	0	0	0	0	0	0
M00001449C:D06	86110	0	0	0	0	0	0
M00001450A:A02	39304	0	0	0	0	0	0
M00001450A:A11	32663	0	0	0	0	0	0
M00001450A:B12	82498	0	0	0	0	0	0
M00001450A:D08	27250	0	0	0	0	0	0
M00001452A:B04	84328	0	0	0	0	0	0
M00001452A:B12	86859	0	0	0	0	0	0
M00001452A:D08	1120	0	0	0	0	0	0
M00001452A:F05	85064	0	0	0	0	0	0
M00001452C:B06	16970	0	0	2	0	1	0
M00001453A:E11	16130	0	0	0	0	0	0
M00001453C:F06	16653	0	0	0	0	0	0
M00001454A:A09	83103	0	0	0	0	0	0
M00001454B:C12	7005	0	0	0	0	0	0
M00001454D:G03	689	0	2	2	0	4	2
M00001455A:E09	13238	0	0	0	0	0	0
M00001455B:E12	13072	0	0	0	0	0	0
M00001455D:F09	9283	0	0	0	0	0	0
M00001455D:F09	9283	0	0	0	0	0	0
M00001460A:F06	2448	0	0	0	0	0	0
M00001460A:F12	39498	0	0	0	0	0	0

Table 6 All Differential Data for Libs 15-20

Table 6 All Differentia			~· .	~· ·		~! ·	~ 1
Clone Name	Cluster	Clones in	Clones in	Clones in	Clones in	Clones in	Clones in
1.6000014614 D06	ID 1521	Lib15	Lib16b	Lib17	Lib18	Lib19 0	Lib20 0
M00001461A:D06	1531	0 2	0 13	0 13	0 0	69	10
M00001463C:B11	19		0		0	0	0
M00001465A:B11	10145	0	=	0	=	0	0
M00001466A:E07	4275	0	0	0	0		
M00001467A:B07	38759	0	0	0	0	0	0
M00001467A:D04	39508	0	0	0	0	0	0
M00001467A:D08	16283	0	0	0	0	0	0
M00001467A:D08	16283	0	0	0	0	0	0
M00001467A:E10	39442	0	0	0	0	0	0
M00001468A:F05	7589	0	0	0	0	0	0
M00001469A:C10	12081	0	0	0	0	0	0
M00001469A:H12	19105	0	0	0	0	0	0
M00001470A:B10	1037	0	0	0	0	0	0
M00001470A:C04	39425	0	0	0	0	0	0
M00001471A:B01	39478	0	0	0	0	0	0
M00001481D:A05	7985	0	0	0	0	0	0
M00001490B:C04	18699	0	0	0	0	0	0
M00001494D:F06	7206	0	0	0	0	0	0
M00001497A:G02	2623	0	0	0	0	0	0
M00001499B:A11	10539	0	0	0	0	0	0
M00001500A:C05	5336	0	0	0	0	0	0
M00001500A:E11	2623	0	0	0	0	0	0
M00001500C:E04	9443	0	0	0	0	0	0
M00001501D:C02	9685	0	0	0	0	0	0
M00001504C:A07	10185	0	0	0	0	0 -	0
M00001504C:H06	6974	0	0	0	0	0	0
M00001504D:G06	6420	0	0	0	0	0	0
M00001507A:H05	39168	0	0	0	0	0	0
M00001511A:H06	39412	0	0	0	0	0	0
M00001512A:A09	39186	0	0	0	0	0	0
M00001512D:G09	3956	0	0	1	0	0	0
M00001513A:B06	4568	0	0	0	0	0	0
M00001513C:E08	14364	0	0	0	0	0	0
M00001514C:D11	40044	0	1	0	0	0	0
M00001517A:B07	4313	0	0	0	0	0	0
M00001518C:B11	8952	0	0	0	0	0	0
M00001528A:C04	7337	0	0	0	0	0	0
M00001528A:F09	18957	0	0	0	0	0	0
M00001528B:H04	8358	0	0	0	0	0	0
M00001531A:D01	38085	0	0	0	0	0	0
M00001532B:A06	3990	1	1	0	0	0	0
M00001533A:C11	2428	0	0	1	0	0	0
M00001534A:C04	16921	0	0	0	0	0	0
M00001534A:D09	5097	0	0	0	0	0	0
M00001534A:F09	5321	0	1	0	0	2	0
M00001534C:A01	4119	0	0	0	0	0	0
M00001535A:B01	7665	0	0	0	0	0	0
M00001535A:C06	20212	0	0	0	0	0	0
M00001535A:E00	39423	0	0	0	0	0	0
	37 123	J	J	J	J	•	,

Table 6 All Differential Data for Libs 15-20

Clone Name Cluster Clones in Clone

Clone Name	Cluster ID	Clones in Lib15	Clones in Lib16b	Clones in Lib17	Clones in Lib18	Clones in Lib19	Clones in Lib20
M00001536A:B07	2696	0	0	0	0	3	0
M00001536A:C08	39392	0	0	0	0	0	0
M00001537A:F12	39420	0	0	0	0	0	0
M00001537B:G07	3389	0	0	0	0	0	0
M00001540A:D06	8286	0	0	0	0	0	0
M00001541A:D02	3765	0	0	0	0	0	0
M00001541A:F07	22085	0	0	0	0	0	0
M00001541A:H03	39174	0	0	0	0	0	0
M00001542A:A09	22113	0	0	0	0	0	0
M00001542A:E06	39453	0	0	0	0	0	0
M00001544A:E03	12170	0	0	0	0	0	0
M00001544A:G02	19829	0	0	0	0	0	0
M00001544B:B07	6974	0	0	0	0	0	0
M00001545A:C03	19255	0	0	0	0	0	0
M00001545A:D08	13864	0	0	0	0	0	0
M00001546A:G11	1267	1	0	0	0	7	0
M00001548A:E10	5892	0	0	0	0	0	0
M00001548A:H09	1058	0	0	1	0	0	0
M00001549A:B02	4015	0	0	0	0	0	0
M00001549A:D08	10944	0	0	0	0	0	0
M00001549B:F06	4193	0	0	0	0	0	0
M00001549C:E06	16347	0	0	0	0	0	0
M00001550A:A03	7239	0	0	0	0	0	0
M00001550A:G01	5175	0	0	0	0	0	0
M00001551A:B10	6268	0	0	0	0	0	0
M00001551A:F05	39180	0	0	0	0	0	0
M00001551A:G06	22390	0	0	0	0	0	0
M00001551C:G09	3266	0	0	1	0	0	0
M00001552A:B12	307	0	0	0	0	3	0
M00001552A:D11	39458	0	0	0	0	0	0
M00001552B:D04	5708	0	1	0	0	0	0
M00001553A:H06	8298	0	0	0	0	0	0
M00001553B:F12	4573	0	0	0	0	0	0
M00001553D:D10	22814	0	0	0	0	0	0
M00001555A:B02	39539	0	0	0	0	0	0
M00001555A:C01	39195	0	0	0	0	0	0
M00001555D:G10	4561	0	0	0	0	0	0
M00001556A:C09	9244	0	0	0	0	0	0
M00001556A:F11	1577	0	0	0	0	0	0
M00001556A:H01	15855	3	5	5	0	3	1
M00001556B:C08	4386	1	2	0	0	0	0
M00001556B:G02	11294	0	$\overline{0}$	0	0	0	0
M00001557A:D02	7065	0	0	0	0	0	0
M00001557A:D02	7065	0	0	0	0	0	0
M00001557A:F01	9635	0	0	0	0	0	0
M00001557A:F01	39490	0	0	0	0	0	0
M00001557A:105	5192	0	0	0	0	0	0
M00001557D:D09	8761	0	0	0	0	0	0
M00001557D:D09	7514	0	0	0	0	0	0
1111.4000100100101111	7317	U	U	U	J	J	J

Clone Name Cluster ID Clones in Lib15 Clones in Lib16b Clones in Lib17 Clones in Lib17 Clones in Lib19 Clones in Lib19 M00001560D:F10 6558 0 0 0 0 0 0 0 M0000156B:F06 102 22 38 65 7 43 10 M0000157B:E364 23001 0 0 0 0 0 0 M0000157B:BE04 23001 0 0 0 0 0 0 M0000157B:BE04 23001 0 0 0 0 0 0 M0000158B:E04 23001 0 0 0 0 0 0 M00001587D:L05 6423 0 0 0 0 0 0 M00001597D:C05 10470 0 0 0 0 0 0 M00001598H:H04 260 0 0 0 0 0 0 M00001698A:G3 16999 <th>Table 6 All Differentia</th> <th>al Data for</th> <th>Libs 15-20</th> <th></th> <th></th> <th></th> <th></th> <th></th>	Table 6 All Differentia	al Data for	Libs 15-20					
M00001560D:F10				Clones in	Clones in	Clones in	Clones in	Clones in
M00001561A:CO5 39486			Lib15	Lib16b		Lib18	Lib19	
M00001563B:F06	M00001560D:F10	6558	0	0	0	0	0	0
M00001564A:B12 5053 0	M00001561A:C05	39486	0	0	0	0	0	0
M00001571C:H06	M00001563B:F06	102	22	38	65	7	43	10
M00001578B:E04 23001 0 0 0 0 0 0 0 0 0	M00001564A:B12	5053	0	0	1	0	0	0
M00001578B:E04 23001 0 0 0 0 0 0 0 0 0	M00001571C:H06	5749	0	0	0	0	0	0
M00001583D:A10 6293 0 0 0 0 0 0 0 0 0	M00001578B:E04	23001	0	0	0	0	0	0
M00001583D:A10 6293 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	M00001579D:C03	6539	0	0	0	0	0	0
M00001586C:C05			0	0	0	0	0	
M00001587A:B11 39380 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0			0	0			1	
M00001594B:H04 260 0 0 0 0 0 0 0 0 0			0	0			0	0
M00001597C:H02 4837 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0			0	0	0	0		
M00001597D:C05 10470 0 0 0 0 0 0 M0000169A:G03 16999 1 1 1 0 0 0 M0000160A:B10 1399 0 0 0 0 0 0 M0000160A:F05 39391 0 0 0 0 0 0 M0000160A:E01 11465 0 0 0 0 0 0 M0000160B:E03 22155 0 0 0 0 0 0 M0000164C:F10 13157 0 0 0 0 0 0 M00001617C:E02 17004 0 0 0 0 0 0 0 M00001621C:C08 40044 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0			0	0				
M00001598A:G03 16999 1 1 1 0 0 0 M00001601A:D08 22794 0 0 0 0 0 0 M00001604A:B10 1399 0 0 0 0 0 0 M00001604A:F05 39391 0 0 0 0 0 0 0 M00001607A:E11 11465 0 0 0 0 0 0 0 M0000168B:E03 22155 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 <td></td> <td></td> <td>0</td> <td>0</td> <td>0</td> <td>0</td> <td></td> <td></td>			0	0	0	0		
M00001601A:D08 22794 0 0 0 0 0 0 M00001604A:B10 1399 0 0 0 0 0 0 M00001607A:E11 11465 0 0 0 0 0 0 M00001608A:B03 7802 0 0 0 0 0 0 M00001618C:F10 13157 0 0 0 0 0 0 M00001619C:F12 17004 0 0 0 0 0 0 M00001619C:F12 40314 0 0 0 0 0 0 M00001621C:C08 40044 0 1 0 0 0 0 0 M00001624C:F01 4309 0 0 0 0 0 0 0 M00001624C:F01 4309 0 0 0 0 0 0 0 0 0 0 0 0 0							_	
M00001604A:B10 1399 0 0 0 0 0 0 M00001604A:F05 39391 0 0 0 0 0 0 M00001608A:B03 7802 0 0 0 0 0 0 M00001608B:E03 22155 0 0 0 0 0 0 M00001614C:F10 13157 0 0 0 0 0 0 M00001617C:E02 17004 0 0 0 0 0 0 M00001621C:C08 40044 0 0 0 0 0 0 0 M00001623D:F10 13913 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0			_	_	=	=	=	
M00001604A:F05 39391 0 0 0 0 0 M00001607A:E11 11465 0 0 0 0 0 M00001608B:B03 7802 0 0 0 0 0 M00001614C:F10 13157 0 0 0 0 0 M00001617C:E02 17004 0 0 0 0 0 M00001619C:F12 40314 0 0 0 0 0 M00001623D:F10 13913 0 0 0 0 0 M00001624A:B06 3277 0 0 0 0 0 M00001624C:F01 4309 0 0 0 0 0 M0000164A:B05 3214 1 0 0 0 0 M0000164SA:C12 19267 0 0 0 0 0 M0000164SC:A01 4665 0 0 0 0 0 M			=	-	-	_	_	
M00001607A:E11 11465 0 0 0 0 0 0 M00001608A:B03 7802 0 0 0 0 0 0 M00001614C:F10 13157 0 0 0 0 0 0 M00001617C:E02 17004 0 0 0 0 0 0 M00001619C:F12 40314 0 0 0 0 0 0 M00001621C:C08 40044 0 1 0 0 0 0 M00001624A:B06 3277 0 0 0 0 0 0 M00001630B:H09 5214 1 0 0 0 0 0 M00001644C:B07 39171 0 0 0 0 0 0 0 M0000164S2:C12 19267 0 0 0 0 0 0 0 0 0 0 0 0 0 0				_	-	_	=	
M00001608A:B03 7802 0 0 0 0 0 M00001608B:E03 22155 0 0 0 0 0 M00001614C:F10 13157 0 0 0 0 0 M00001617C:E02 17004 0 0 0 0 1 0 M00001619C:F12 40314 0 0 0 0 0 0 M00001621C:C08 40044 0 1 0 0 0 0 M00001623D:F10 13913 0 0 0 0 0 0 M00001624A:B06 3277 0 0 0 0 0 0 M00001624C:F01 4309 0 0 0 0 0 0 M0000164C:F01 4309 0 0 0 0 0 0 M0000164C:B07 39171 0 0 0 0 0 0 M00001657D:C03 <td></td> <td></td> <td>=</td> <td>_</td> <td></td> <td></td> <td></td> <td></td>			=	_				
M00001608B:E03 22155 0 0 0 0 0 0 M00001614C:F10 13157 0 0 0 0 0 0 M00001617C:E02 17004 0 0 0 0 1 0 M00001621C:C08 40044 0 1 0 0 0 0 M00001623D:F10 13913 0 0 0 0 0 0 M00001624A:B06 3277 0 0 0 0 0 0 M00001624C:F01 4309 0 0 0 0 0 0 M00001630B:H09 5214 1 0 0 1 1 0 M0000164C:B07 39171 0 0 0 0 0 0 M00001648C:A01 4665 0 0 0 0 0 0 M00001657D:F08 76760 0 0 0 0 0 <t< td=""><td></td><td></td><td>_</td><td></td><td></td><td>-</td><td>_</td><td>=</td></t<>			_			-	_	=
M00001614C:F10 13157 0 0 0 0 0 M00001617C:E02 17004 0 0 0 0 1 0 M00001619C:F12 40314 0 0 0 0 0 0 M00001621C:C08 40044 0 1 0 0 0 0 M00001621C:C08 40044 0 1 0 0 0 0 M00001624A:B06 3277 0 0 0 0 0 0 M00001630B:H09 5214 1 0 0 0 0 0 M00001644C:B07 39171 0 0 0 0 0 0 M00001648C:A01 4665 0 0 0 0 0 0 M00001657D:F08 76760 0 0 0 0 0 0 M00001669B:F02 6468 0 0 0 0 0 0			_	-			_	_
M00001617C:E02 17004 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0			_				=	_
M00001619C:F12 40314 0 0 0 0 0 M00001621C:C08 40044 0 1 0 0 0 M00001623D:F10 13913 0 0 0 0 0 M00001624A:B06 3277 0 0 0 0 0 M00001624C:F01 4309 0 0 0 0 0 M00001630B:H09 5214 1 0 0 1 1 0 M00001644C:B07 39171 0 0 0 0 0 0 0 M00001645A:C12 19267 0 0 0 0 0 0 0 M00001648C:A01 4665 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0			_				=	_
M00001621C:C08 40044 0 1 0 0 0 M00001623D:F10 13913 0 0 0 0 0 M00001624A:B06 3277 0 0 0 0 0 M00001624C:F01 4309 0 0 0 0 0 M00001630B:H09 5214 1 0 0 1 1 0 M00001644C:B07 39171 0 0 0 0 0 0 M00001648C:A01 4665 0 0 0 0 0 0 M00001657D:C03 23201 0 0 0 0 0 0 M00001657D:F08 76760 0 0 0 0 0 0 M00001667D:F08 76760 0 0 0 0 0 0 M00001669B:F02 6468 0 0 0 0 0 0 M00001679C:H02 1436				=			=	
M00001623D:F10 13913 0 0 0 0 0 0 M00001624A:B06 3277 0 0 0 0 0 0 M00001624C:F01 4309 0 0 0 0 0 0 M00001630B:H09 5214 1 0 0 1 1 0 M00001647C:B07 39171 0 0 0 0 0 0 M00001645A:C12 19267 0 0 0 0 1 0 M00001648C:A01 4665 0 0 0 0 0 0 M00001657D:F08 76760 0 0 0 0 0 0 M00001662C:A09 23218 0 0 0 0 0 0 M00001669B:F02 6468 0 0 0 0 0 0 M00001670C:H02 14367 0 0 0 0 0 <t< td=""><td></td><td></td><td>_</td><td>_</td><td>-</td><td>_</td><td>_</td><td></td></t<>			_	_	-	_	_	
M00001624A:B06 3277 0 0 0 0 0 0 M00001624C:F01 4309 0 0 0 0 0 0 M00001630B:H09 5214 1 0 0 1 1 0 M00001644C:B07 39171 0 0 0 0 0 0 M0000164SC:A01 4665 0 0 0 0 0 0 M00001657D:C03 23201 0 0 0 0 0 0 M00001657D:F08 76760 0 0 0 0 0 0 M00001662C:A09 23218 0 0 0 0 0 0 M00001663A:E04 35702 0 0 0 0 0 0 M00001670C:H02 14367 0 0 0 0 0 0 M00001675A:C09 8773 0 0 0 0 0 <t< td=""><td></td><td></td><td>-</td><td>_</td><td></td><td></td><td>-</td><td>-</td></t<>			-	_			-	-
M00001624C:F01 4309 0 0 0 0 0 M00001630B:H09 5214 1 0 0 1 1 0 M00001644C:B07 39171 0 0 0 0 0 0 M00001645A:C12 19267 0 0 0 0 1 0 M00001648C:A01 4665 0 0 0 0 0 0 M00001657D:C03 23201 0 0 0 0 0 0 M00001657D:F08 76760 0 0 0 0 0 0 M00001662C:A09 23218 0 0 0 0 0 0 M00001663A:E04 35702 0 0 0 0 0 0 M00001679C:H02 14367 0 0 0 0 0 0 M0000167SA:C09 8773 0 0 0 0 0 0			=	_			_	
M00001630B:H09 5214 1 0 0 1 1 0 M00001644C:B07 39171 0 0 0 0 0 0 M00001645A:C12 19267 0 0 0 0 1 0 M00001648C:A01 4665 0 0 0 0 0 0 M00001657D:C03 23201 0 0 0 0 0 0 M00001657D:F08 76760 0 0 0 0 0 0 M00001662C:A09 23218 0 0 0 0 0 0 M00001663A:E04 35702 0 0 0 0 0 0 M00001669B:F02 6468 0 0 0 0 0 0 M00001670C:H02 14367 0 0 0 0 0 0 M00001673C:H02 7015 0 0 0 0 0 <			=	-			_	
M00001644C:B07 39171 0 0 0 0 0 M00001645A:C12 19267 0 0 0 0 1 0 M00001648C:A01 4665 0 0 0 0 0 0 M00001657D:C03 23201 0 0 0 0 0 0 M00001657D:F08 76760 0 0 0 0 0 0 M00001657D:F08 76760 0 0 0 0 0 0 M00001657D:F08 76760 0 0 0 0 0 0 M00001662C:A09 23218 0 0 0 0 0 0 M00001663A:E04 35702 0 0 0 0 0 0 M00001669B:F02 6468 0 0 0 0 0 0 0 M00001670C:H02 14367 0 0 0 0 0				=			=	
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M00001657D:F08 76760 0 0 0 0 0 0 M00001662C:A09 23218 0 0 0 0 0 0 M00001663A:E04 35702 0 0 0 0 0 0 M00001669B:F02 6468 0 0 0 0 0 0 M00001670C:H02 14367 0 0 0 0 0 0 M00001673C:H02 7015 0 0 0 0 0 0 M00001675A:C09 8773 0 0 0 0 0 0 M00001676B:F05 11460 0 0 0 0 0 0 M00001677C:E10 14627 0 1 0 0 0 0 M00001678D:F12 4416 0 0 0 0 0 0 M00001679A:F10 26875 0 0 0 0 0 0 M00001679B:F01 6298 0 0 0 0 0			_	=	_	_		
M00001662C:A09 23218 0 0 0 0 0 0 M00001663A:E04 35702 0 0 0 0 0 0 M00001669B:F02 6468 0 0 0 0 0 0 M00001670C:H02 14367 0 0 0 0 0 0 M00001673C:H02 7015 0 0 0 0 0 0 M00001675A:C09 8773 0 0 0 0 0 0 M00001676B:F05 11460 0 0 0 0 0 0 M00001677C:E10 14627 0 1 0 0 0 0 M00001679D:F12 4416 0 0 0 0 0 0 M00001679A:F10 26875 0 0 0 0 0 0 M00001679B:F01 6298 0 0 0 0 0 <t< td=""><td></td><td></td><td>_</td><td>_</td><td>_</td><td>_</td><td>_</td><td></td></t<>			_	_	_	_	_	
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M00001670C:H02 14367 0 0 0 0 0 0 M00001673C:H02 7015 0 0 0 0 0 0 M00001675A:C09 8773 0 0 0 0 0 0 M00001676B:F05 11460 0 0 0 0 0 0 M00001677C:E10 14627 0 1 0 0 0 0 M00001677D:A07 7570 0 0 0 0 0 0 M00001678D:F12 4416 0 0 0 0 0 0 M00001679A:A06 6660 0 0 0 0 0 0 M00001679B:F01 6298 0 0 0 0 0 0								
M00001673C:H02 7015 0 0 0 0 0 0 M00001675A:C09 8773 0 0 0 0 0 0 0 M00001676B:F05 11460 0 0 0 0 0 0 0 M00001677C:E10 14627 0 1 0 0 0 0 0 M00001677D:A07 7570 0 0 0 0 0 0 0 M00001678D:F12 4416 0 0 0 0 0 0 0 M00001679A:A06 6660 0 0 0 0 0 0 0 M00001679B:F01 6298 0 0 0 0 0 0 0								
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M00001676B:F05 11460 0 0 0 0 0 0 M00001677C:E10 14627 0 1 0 0 0 0 0 M00001677D:A07 7570 0 0 0 0 0 0 0 M00001678D:F12 4416 0 0 0 0 0 0 0 M00001679A:A06 6660 0 0 0 0 0 0 0 M00001679A:F10 26875 0 0 0 0 0 0 0 M00001679B:F01 6298 0 0 0 0 0 0 0								
M00001677C:E10 14627 0 1 0 0 0 0 M00001677D:A07 7570 0 0 0 0 0 0 0 M00001678D:F12 4416 0 0 0 0 0 0 0 M00001679A:A06 6660 0 0 0 0 0 0 0 M00001679A:F10 26875 0 0 0 0 0 0 0 M00001679B:F01 6298 0 0 0 0 0 0 0								
M00001677D:A07 7570 0 0 0 0 0 0 M00001678D:F12 4416 0 0 0 0 0 0 M00001679A:A06 6660 0 0 0 0 0 0 M00001679A:F10 26875 0 0 0 0 0 0 M00001679B:F01 6298 0 0 0 0 0 0								
M00001678D:F12 4416 0 0 0 0 0 0 M00001679A:A06 6660 0 0 0 0 0 0 0 M00001679A:F10 26875 0 0 0 0 0 0 M00001679B:F01 6298 0 0 0 0 0 0								
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M00001679A:F10 26875 0 0 0 0 0 0 0 M00001679B:F01 6298 0 0 0 0 0								
M00001679B:F01 6298 0 0 0 0 0			-				=	
			_				0	
M00001679C:F01 78091 0 0 0 0 0 0			0				_	
			0					0
M00001679D:D03 10751 0 0 0 0 0			0		0		0	0
M00001679D:D03 10751 0 0 0 0 0 0	M00001679D:D03	10751	0	0	0	0	0	0

Table 6 All Differential	l Data for l	Libs 15-20					
	Cluster	Clones in	Clones in	Clones in	Clones in	Clones in	Clones in
	ID	Lib15	Lib16b	Lib17	Lib18	Lib19	Lib20
M00001680D:F08	10539	0	0	0	0	0	0
M00001682C:B12	17055	0	0	0	0	0	0
M00001686A:E06	4622	0	0	0	0	0	0
M00001688C:F09	5382	0	0	0	0	0	0
M00001693C:G01	4393	0	0	0	0	0	0
M00001716D:H05	67252	0	0	0	0	0	0
M00003741D:C09	40108	0	0	0	0	0	0
M00003747D:C05	11476	0	0	0	0	0	0
M00003759B:B09	697	0	0	0	0	1	0
M00003762C:B08	17076	0	0	0	0	0	0
M00003763A:F06	3108	0	0	0	0	0	0
M00003774C:A03	67907	0	0	0	0	0	0
M00003796C:D05	5619	. 0	0	0	0	0	0
M00003826B:A06	11350	0	0	0	0	0	0
M00003833A:E05	21877	0	0	0	0	0	0
M00003837D:A01	7899	0	0	0	0	0	0
M00003839A:D08	7798	0	0	0	0	0	0
M00003844C:B11	6539	0	0	0	0	0	0
M00003846B:D06	6874	0	0	1	0	0	0
M00003851B:D10	13595	0	0	0	0	0	0
M00003853A:D04	5619	0	0	0	0	0	0
M00003853A:F12	10515	0	0	0	0	0	0
M00003856B:C02	4622	0	o 0	0	0	0	0
M00003857A:G10	3389	0	0	0	0	0	0
M00003857A:H03	4718	0	0	0	0	0	0
M00003871C:E02	4573	0	0	0	0	0	0
M00003875B:F04	12977	0	0	0	0	0	0
M00003875B:F04	12977	0	0	0	0	0	0
M00003875C:G07	8479	0	0	0	0	0	1
M00003876D:E12	7798	0	0	0	0	0	0
M00003879B:C11	5345	0	0	0	2	0	1
M00003879B:D10	31587	0	0	0	0	0	0
M00003879D:A02	14507	0	0	0	0	0	0
M00003879D:A02	13576	0	0	0	0	0	0
M00003885C:A02	13576	0	0	0	0	0	0
M00003865C:A02	9285	0	0	0	0	0	0
M00003900C.E10	39809	0	0	0	0	0	0
M00003907D:H04	16317	0	0	0	0	0	0
			0	0	0	0	0
M00003909D:C03	8 672	• 0					
M00003912B:D01	12532	0	0	0	0	0	0
M00003914C:F05	3900	0	0	0	0	1	0
M00003922A:E06	23255	0	0	0	0	0	0
M00003958A:H02	18957	0	0	0	0	0	0
M00003958A:H02	18957	0	0	0	0	0	0
M00003958C:G10	40455	0	0	0	0	0	0
M00003958C:G10	40455	0	0	0	0	0	0
M00003968B:F06	24488	0	0	0	0	0	0
M00003970C:B09	40122	0	0	0	0	0	0
M00003974D:E07	23210	0	0	0	0	0	0

Table 6 All Differential Data for Libs 15-20

Clone Name	Cluster ID	Clones in Lib15	Clones in Lib16b	Clones in Lib17	Clones in Lib18	Clones in Lib19	Clones in Lib20
M00003974D:H02	23358	0	0	0	0	0	0
M00003975A:G11	12439	0	0	0	0	0	0
M00003978B:G05	5693	0	0	0	0	0	0
M00003981A:E10	3430	0	0	0	0	1	0
M00003982C:C02	2433	0	0	0	0	0	0
M00003983A:A05	9105	0	0	0	0	0	0
M00004028D:A06	6124	0	0	0	0	0	0
M00004028D:C05	40073	0	0	0	0	0	0
M00004031A:A12	9061	0	0	0	0	0	0
M00004031A:A12	9061	0	0	0	0	0	0
M00004035C:A07	37285	0	0	0	0	0	0
M00004035D:B06	17036	0	0	0	0	0	0
M00004059A:D06	5417	0	0	0	0	0	0
M00004068B:A01	3706	0	0	0	Ō	0	0
M00004072B:B05	17036	0	0	0	0	0	0
M00004081C:D10	15069	0	0	0	0	0	0
M00004081C:D12	14391	o O	0	0	0	0	0
M00004086D:G06	9285	0	0	0	0	0	Ő
M00004087D:A01	6880	o 0	Ö	0	0	0	0
M00004093D:B12	5325	1	1	Ö	1	0	1
M00004093D:B12	5325	1	1	Ö	1	0	1
M00004095D:B12	7221	0	0	Ö	0	0	0
M00004108A:E06	4937	0	0	0	0	0	0
M0000410571:E00	6874	0	0	1	0	0	ő
M000041112:700	13183	0	0	0	0	0	Ŏ
M00004114E:F11	13272	0	0	0	0	0	ő
M00004136D:H02	5257	0	1	ő	0	0	ŏ
M00004140C:C11	16977	0	0	0	0	0	0
M00004157D:B00	6455	0	0	0	0	0	0
M00004169C:C12	5319	0	0	0	0	0	Ŏ
M00004109C:C12	4908	0	0	0	0	0	0
M00004171D:B03	11494	0	0	0	0	0	o 0
M00004172C:D00 M00004183C:D07	16392	0	0	0	0	0	0
M00004185C:C03	11443	0	0	0	0	0	0
M00004197D:H01	8 210	0	0	0	0	0	0
M00004197B:R101 M00004203B:C12	14311	0	0	0	0	0	0
M00004203B:C12	2379	0	0	0	0	0	0
M00004212B:C07	11451	0	0	0	0	0	0
M00004214C:1103	16918	0	0	0	0	0	0
M00004223A:010	7 89 9	0	0	0	0	0	0
M00004223D:E04	12971	0	0	0	0	0	0
M00004223D:E04 M00004229B:F08	6455	0	0	0	0	0	0
M00004229B.F08 M00004230B:C07	7212	0	0	0	0	0	0
M00004250B:C07 M00004269D:D06		_			0		
	4905	0	0	0	0	0	0 0
M00004275C:C11	16914	0	0	0	-	0	
M00004283B:A04	14286	0	0	0	0	0	0
M00004285B:E08	56020	0	0	0	0	0	0
M00004295D:F12	16921	0	0	0	0	0	0
M00004296C:H07	13046	0	0	0	0	0	0

Table 6 All Differential Data for Libs 15-20

Cluster	Clones in	Clones in	Clones in	Clones in	Clones in	Clones in
ID	Lib15	Lib16b	Lib17	Lib18	Lib19	Lib20
9457	0	0	0	0	0	0
26295	0	0	0	0	0	0
21847	0	0	0	0	0	0
2030	0	0	0	0	0	0
2102	0	0	0	0	0	0
	ID 9457 26295 21847 2030	ID Lib15 9457 0 26295 0 21847 0 2030 0	ID Lib15 Lib16b 9457 0 0 26295 0 0 21847 0 0 2030 0 0	ID Lib15 Lib16b Lib17 9457 0 0 0 26295 0 0 0 21847 0 0 0 2030 0 0 0	ID Lib15 Lib16b Lib17 Lib18 9457 0 0 0 0 26295 0 0 0 0 21847 0 0 0 0 2030 0 0 0 0	ID Lib15 Lib16b Lib17 Lib18 Lib19 9457 0 0 0 0 0 26295 0 0 0 0 0 21847 0 0 0 0 0 2030 0 0 0 0 0

Table 7 All Differential Data for Libs 12-14

Clone Name	Cluster ID	Clones in Lib12	Clones in Lib13	Clones in Lib14
M00001340B:A06	17062	0	0	0
M00001340D:F10	115 8 9	0	0	0
M00001341A:E12	4443	4	2	0
M00001342B:E06	39805	0	0	0
M00001343C:F10	2790	0	0	0
M00001343D:H07	23255	0	0	0
M00001345A:E01	6420	0	0	0
M00001346A:F09	5007	0	0	0
M00001346D:E03	6806	0	1	1
M00001346D:G06	5779	0	0	0
M00001346D:G06	5779	0	0	0
M00001347A:B10	13576	0	0	0
M00001348B:B04	16927	0	0	0
M00001348B:G06	16985	0	0	0
M00001349B:B08	35 8 4	0	0	0
M00001350A:H01	7187	0	0	0
M00001351B:A08	3162	0	. 0	1
M00001351B:A08	3162	0	0	1
M00001352A:E02	16245	0	0	0
M00001353A:G12	8078	0	0	0
M00001353D:D10	14929	0	1	0
M00001355B:G10	14391	0	0	0
M00001357D:D11	4059	0	0	0
M00001361A:A05	4141	1	2	1
M00001361D:F08	2379	0	0	0
M00001362B:D10	5622	0	2	1
M00001362C:H11	945	0	0	0
M00001365C:C10	40132	0	0	0
M00001370A:C09	6867	0	0	0
M00001371C:E09	7172	0	0	1
M00001376B:G06	17732	2	0	0
M00001378B:B02	39833	0	0	0
M00001379A:A05	1334	0	0	0
M00001380D:B09	39886	0	0	0
M00001382C:A02	22979	1	0	0
M00001383A:C03	39648	0	0	0
M00001383A:C03	39648	0	0	0
M00001386C:B12	5178	0	0	0
M00001387A:C05	2464	0	0	0
M00001387B:G03	7587	o	0	0
M00001387D:G05	5832	o	0	0
M00001389A:C08	16269	2	0	0
M00001389A:C08	6583	0	0	0
M00001394A:F01 M00001395A:C03	4016	0	0	0
M00001395A.C03	4009	2	0	0
M00001390A.C03	39563	0	0	0
M00001402A.E08 M00001407B:D11	5556	0	0	0
14170701140/D'IJ	<i>333</i> 0	v	U	J

Table 7 All Differential Data for Libs 12-14

Clone Name	Cluster ID	Clones in Lib12	Clones in Lib13	Clones in Lib14
M00001409C:D12	9577	0	0	0
M00001410A:D07	7005	0	0	0
M00001412B:B10	8 551	0	0	0
M00001415A:H06	13538	0	0	0
M00001416A:H01	7674	0	0	0
M00001416B:H11	8847	1	0	0
M00001417A:E02	36393	0	0	0
M00001418B:F03	9952	0	0	0
M00001418D:B06	8526	0	0	0
M00001421C:F01	9577	0	0	0
M00001423B:E07	15066	0	0	0
M00001424B:G09	10470	0	0	0
M00001425B:H08	22195	0	0	0
M00001426D:C08	4261	0	0	0
M00001428A:H10	84182	0	0	0
M00001429A:H04	2797	0	0	0
M00001429B:A11	4635	0	0	0
M00001429D:D07	40392	0	0	0
M00001439C:F08	40054	0	0	0
M00001442C:D07	16731	0	0	0
M00001445A:F05	13532	0	0	0
M00001446A:F05	78 01	0	1	0
M00001447A:G03	10717	0	0	0
M00001448D:C09	8	7	6	9
M00001448D:H01	36313	1	0	0
M00001449A:A12	5857	0	0	0
M00001449A:B12	41633	0	0	0
M00001449A:D12	3681	1	0	0
M00001449A:G10	36535	0	0	0
M00001449C:D06	86110	0	0	0
M00001450A:A02	39304	0	1	0
M00001450A:A11	32663	0	0	0
M00001450A:B12	82498	0	0	0
M00001450A:D08	27250	0	0	0
M00001452A:B04	84328	0	0	0
M00001452A:B12	86859	0	0	0
M00001452A:D08	1120	0	0	0
M00001452A:F05	85064	0	0	0
M00001452C:B06	16970	1	0	0
M00001453A;E11	16130	0	0	0
M00001453C:F06	16653	0	0	0
M00001454A:A09	83103	0	0	0
M00001454B:C12	7005	0	0	0
M00001454D:G03	689	0	0	1
M00001455A:E09	13238	0	0	0
M00001455B:E12	13072	Ö	0	Ö
M00001455D:E12	9283	Ö	0	0
M00001455D:F09	9283	ő	0	0
	, 200	·	~	-

Table 7 All Differential Data for Libs 12-14

Clone Name	Cluster ID	Clones in Lib12	Clones in Lib13	Clones in Lib14
M00001460A:F06	2448	0	0	0
M00001460A:F12	39498	0	0	0
M00001461A:D06	1531	0	0	1
M00001463C:B11	19	17	32	31
M00001465A:B11	10145	0	0	0
M00001466A:E07	4275	0	0	0
M00001467A:B07	38759	0	0	0
M00001467A:D04	39508	0	0	0
M00001467A:D08	16283	0	0	0
M00001467A:D08	16283	0	0	0
M00001467A:E10	39442	0	0	0
M00001468A:F05	7589	0	0	0
M00001469A:C10	12081	0	0	0
M00001469A:H12	19105	0	0	0
M00001470A:B10	1037	0	0	0
M00001470A:C04	39425	0	0	0
M00001471A:B01	39478	0	0	0
M00001481D:A05	7985	0	0	0
M00001490B:C04	18699	0	0	0
M00001494D:F06	7206	0	0	0
M00001497A:G02	2623	1	0	0
M00001499B:A11	10539	0	1	0
M00001500A:C05	5336	0	0	0
M00001500A:E11	2623	1	0	0
M00001500C:E04	9443	0	0	0
M00001501D:C02	9685	0	0	0
M00001504C:A07	10185	0	0	0
M00001504C:H06	6974	0	0	0
M00001504D:G06	6420	0	0	0
M00001507A:H05	39168	0	0	0
M00001511A:H06	39412	0	0	0
M00001512A:A09	39186	0	0	0
M00001512D:G09	3956	0	0	0
M00001513A:B06	4568	0	0	0
M00001513C:E08	14364	0	0	0
M00001514C:D11	40044	0	0	0
M00001517A:B07	4313	0	0	0
M00001518C:B11	8952	0	0	0
M00001528A:C04	7337	1	2	2
M00001528A:F09	18957	0	0	0
M00001528B:H04	8358	0	0	0
M00001531A:D01	38085	0	0	0
M00001532B:A06	3990	0	0	0
M00001533A:C11	2428	. 0	0	0
M00001534A:C04	16921	0	0	0
M00001534A:D09	5097	0	0	0
M00001534A:F09	5321	4	7	6
M00001534C:A01	4119	0	0	0

Table 7 All Differential Data for Libs 12-14

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M00001535A:B01	7665	0	2	4
M00001535A:C06	20212	0	0	0
M00001535A:F10	39423	0	0	0
M00001536A:B07	2696	0	0	0
M00001536A:C08	39392	0	0	0
M00001537A:F12	39420	0	0	0
M00001537B:G07	3389	0	0	0
M00001540A:D06	8286	0	0	0
M00001541A:D02	3765	0	0	0
M00001541A:F07	22085	0	0	0
M00001541A:H03	39174	0	0	0
M00001542A:A09	22113	0	0	0
M00001542A:E06	39453	0	0	0
M00001544A:E03	12170	0	0	0
M00001544A:G02	19829	0	0	0
M00001544B:B07	6974	0	0	0
M00001545A:C03	19255	0	0	0
M00001545A:D08	13864	0	0	0
M00001546A:G11	1267	0	0	0
M00001548A:E10	5892	0	1	0
M00001548A:H09	1058	1	3	0
M00001549A:B02	4015	0	1	0
M00001549A:D08	10944	1	0	0
M00001549B:F06	4193	0	0	0
M00001549C:E06	16347	0	0	0
M00001550A:A03	7239	0	1	0
M00001550A:G01	5175	1	0	0
M00001551A:B10	6268	0	0	1
M00001551A:F05	39180	0	0	0
M00001551A:G06	22390	0	0	1
M00001551C:G09	3266	0	0	0
M00001552A:B12	307	6	11	4
M00001552A:D11	39458	0	0	0
M00001552B:D04	5708	0	0	0
M00001553A:H06	8298	0	0	0
M00001553B:F12	4573	0	0	0
M00001553D:D10	22814	0	0	0
M00001555A:B02	39539	0	0	0
M00001555A:C01	39195	0	0	0
M00001555D:G10	4561	0	0	0
M00001556A:C09	9244	0	1	0
M00001556A:F11	1577	0	0	2
M00001556A:H01	15855	1	1	0
M00001556B:C08	4386	3	0	1
M00001556B:G02	11294	0	0	0
M00001550B:G02	7065	Ö	o	o
M00001557A:D02	7065	0	0	0
M00001557A:E02	9635	Ö	ő	o
	, ,,,,	~	-	~

Table 7 All Differential Data for Libs 12-14

Clone Name	Cluster ID	Clones in Lib12	Clones in Lib13	Clones in Lib14
M00001557A:F03	39490	0	0	0
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M00001557D:D09	876 1	0	0	0
M00001558B:H11	7514	0	0	0
M00001560D:F10	6558	0	0	0
M00001561A:C05	39486	0	0	0
M00001563B:F06	102	2	1	2
M00001564A:B12	5053	0	0	0
M00001571C:H06	5749	0	0	0
M00001578B:E04	23001	0	0	0
M00001579D:C03	6539	0	0	0
M00001583D:A10	6293	0	0	0
M00001586C:C05	4623	0	0	0
M00001587A:B11	39380	0	0	0
M00001594B:H04	260	1	0	0
M00001597C:H02	4837	1	0	0
M00001597D:C05	10470	0	0	0
M00001598A:G03	16999	4	2	6
M00001601A:D08	22794	0	0	0
M00001604A:B10	1399	6	3	3
M00001604A:F05	39391	0	0	0
M00001607A:E11	11465	0	0	0
M00001608A:B03	7802	0	0	0
M00001608B:E03	22155	0	0	0
M00001614C:F10	13157	0	0	0
M00001617C:E02	17004	0	0	0
M00001619C:F12	40314	0	0	0
M00001621C:C08	40044	0	0	0
M00001623D:F10	13913	0	0	0
M00001624A:B06	3277	0	0	0
M00001624C:F01	4309	0	0	0
M00001630B:H09	5214	0	1	2
M00001644C:B07	39171	0	0	0
M00001645A:C12	19267	0	0	0
M00001648C:A01	4665	0	0	0
M00001657D:C03	23201	0	0	0
M00001657D:F08	76760	0	0	0
M00001662C:A09	23218	0	0	0
M00001663A:E04	35702	0	0	0
M00001669B:F02	6468	0	0	0
M00001670C:H02	14367	0	0	0
M00001673C:H02	7015	0	0	0
M00001675A:C09	8773	0	0	0
M00001676B:F05	11460	2	0	0
M00001677C:E10	14627	0	0	0
M00001677D:A07	7570	0	0	0
M00001678D:F12	4416	1	2	0
M00001679A:A06	6660	0	0	0

Table 7 All Differential Data for Libs 12-14

Clone Name	Cluster ID	Clones in Lib12	Clones in Lib13	Clones in Lib14
M00001679A:F10	26875	0	0	0
M00001679B:F01	6298	0	0	0
M00001679C:F01	78091	0	0	0
M00001679D:D03	10751	0	0	0
M00001679D:D03	10751	0	0	0
M00001680D:F08	10539	0	1	0
M00001682C:B12	17055	0	0	0
M00001686A:E06	4622	0	0	0
M00001688C:F09	5382	0	0	0
M00001693C:G01	4393	0	0	0
M00001716D:H05	67252	0	0	0
M00003741D:C09	40108	0	0	0
M00003747D:C05	11476	0	0	0
M00003759B:B09	697	0	0	0
M00003762C:B08	17076	0	0	0
M00003763A:F06	3108	0	0	0
M00003774C:A03	67907	0	0	0
M00003796C:D05	5619	0	1	0
M00003826B:A06	11350	0	0	0
M00003833A:E05	21877	0	0	0
M00003837D:A01	7899	0	0	0
M00003839A:D08	7798	0	0	0
M00003844C:B11	6539	0	0	0
M00003846B:D06	6874	0	0	0
M00003851B:D10	13595	0	0	0
M00003853A:D04	5619	0	1	0
M00003853A:F12	10515	0	0	1
M00003856B:C02	4622	0	0	0
M00003857A:G10	3389	0	0	0
M00003857A:H03	4718	0	0	0
M00003871C:E02	4573	0	0	0
M00003875B:F04	12977	0	0	0
M00003875B:F04	12977	0	0	0
M00003875C:G07	8 479	1	0	0
M00003876D:E12	7798	0	0	0
M00003879B:C11	5345	4	8	3
M00003879B:D10	31587	0	0	0
M00003879D:A02	14507	0	0	0
M00003885C:A02	13576	0	0	0
M00003885C:A02	13576	0	0	0
M00003906C:E10	9285	0	0	0
M00003907D:A09	39809	0	0	0
M00003907D:H04	16317	0	0	0
M00003909D:C03	8672	0	0	0
M00003912B:D01	12532	0	0	0
M00003914C:F05	3900	0	1	0
M00003922A:E06	23255	0	0	0
M00003958A:H02	18957	0	0	0

Table 7 All Differential Data for Libs 12-14

Clone Name	Cluster ID	Clones in	Clones in	Clones in
		Lib12	Lib13	Lib14
M00003958A:H02	18957	0	0	0
M00003958C:G10	40455	0	0	0
M00003958C:G10	40455	0	0	0
M00003968B:F06	24488	0	0	0
M00003970C:B09	40122	0	0	0
M00003974D:E07	23210	ő	0	0
M00003974D:B07	23358	0	0	0
M00003975A:G11	12439	ő	0	o
M00003978B:G05	5693	ő	0	ő
M00003970B:G09	3430	ő	Ö	ő
M0000398171:210	2433	2	4	ő
M00003983A:A05	9105	0	0	0
M00003783A:A03	6124	0	0	0
M00004028D:A00 M00004028D:C05	40073	0	1	0
M00004020D:C03	9061	0	0	ő
M00004031A:A12	9061	0	0	Ö
M00004031A:A12	37285	0	0	0
M00004035C:A07 M00004035D:B06	17036	0	0	0
M00004055D.B00 M00004059A:D06	5417	0	0	0
M00004059A:D00 M00004068B:A01	3706	0	0	0
			0	0
M00004072B:B05	17036	0		0
M00004081C:D10	15069	0	0	
M00004081C:D12	14391	0	0 .	0
M00004086D:G06	9285	0	0	0
M00004087D:A01	6880	0	0	0
M00004093D:B12	5325	0	0	0
M00004093D:B12	5325	0	0	0
M00004105C:A04	7221	0	0	0
M00004111R A08	4937	0	0	0
M00004111D:A08	6874	0	0	0
M00004114C:F11	13183	0	0	0
M00004138B:H02	13272	0	0	0
M00004146C:C11	5257	0	0	1
M00004151D:B08	16977	0	0	0
M00004157C:A09	6455	0	0	0
M00004169C:C12	5319	0	0	0
M00004171D:B03	4908	0	0	0
M00004172C:D08	11494	0	0	0
M00004183C:D07	16392	0	0	0
M00004185C:C03	11443	2	0	0
M00004197D:H01	8210	0	0	0
M00004203B:C12	14311	0	0	0
M00004212B:C07	2379	0	0	0
M00004214C:H05	11451	0	0	0
M00004223A:G10	16918	0	0	0
M00004223B:D09	7899	0	0	0
M00004223D:E04	12971	0	0	0
M00004229B:F08	6455	0	0	0

Table 7 All Differential Data for Libs 12-14

Clone Name	Cluster ID	Clones in Lib12	Clones in Lib13	Clones in Lib14
M00004230B:C07	7212	0	0	1
M00004269D:D06	4905	0	0	0
M00004275C:C11	16914	0	0	0
M00004283B:A04	14286	0	0	0
M00004285B:E08	56020	0	0	0
M00004295D:F12	16921	0	0	0
M00004296C:H07	13046	0	0	0
M00004307C:A06	9457	1	0	0
M00004312A:G03	26295	0	0	0
M00004318C:D10	21847	0	0	0
M00004372A:A03	2030	0	0	0
M00004377C:F05	2102	0	0	0

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We Claim:

1. A library of polynucleotides, the library comprising the sequence information of at least one of SEQ ID NOS:1-844.

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- 2. The library of claim 1, wherein the library is provided on a nucleic acid array.
- 3. The library of claim 1, wherein the library is provided in a computer-readable format.

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- 4. The library of claim 1, wherein the library comprises a differentially expressed polynucleotide comprising a sequence selected from the group consisting of SEQ ID NOS:9, 39, 42, 52, 62, 74, 119, 172, 317, and 379.
- 5. The library of claim 1, wherein the library comprises a polynucleotide differentially expressed in a human breast cancer cell, where the polynucleotide comprises a sequence selected from the group consisting of SEQ ID NOS: 4, 9, 39, 42, 52, 62, 65, 66, 68, 74, 81, 114, 123, 144, 130, 157, 162, 172, 178, 183, 202, 214, 219, 223, 258, 298, 317, 338, 379, 384, 386, and 388.

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6. The library of claim 1, wherein the library comprises a polynucleotide differentially expressed in a human colon cancer cell, where the polynucleotide comprises a sequence selected from the group consisting of SEQ ID NOS: 1, 39, 52, 97, 119, 134, 172, 176, 241, 288, 317, 357, 362, and 374.

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7. The library of claim 1, wherein the library comprises a polynucleotide differentially expressed in a human lung cancer cell, where the polynucleotide comprises a sequence selected from the group consisting of SEQ ID NOS: 9, 34, 42, 62, 74, 106, 119, 135, 154, 160, 260, 308, 323, 349, 361, 369, 371, 379, 395, 381, and 400.

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8. An isolated polynucleotide comprising a nucleotide sequence having at least 90% sequence identity to an identifying sequence of SEQ ID NOS:1-844 or a degenerate variant thereof.

9. An isolated polynucleotide according to claim 8, wherein the polynucleotide comprises a sequence encoding a polypeptide of a protein family selected from the group consisting of: 4 transmembrane segments integral membrane proteins, 7 transmembrane receptors, ATPases associated with various cellular activities (AAA), eukaryotic aspartyl proteases, GATA family of transcription factors, G-protein alpha subunit, phorbol esters/diacylglycerol binding proteins, protein kinase, protein phosphatase 2C, protein tyrosine phosphatase, trypsin, wnt family of developmental signaling proteins, and WW/rsp5/WWP domain containing proteins.

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10. The polynucleotide of claim 9, wherein the polynucleotide comprises a sequence of one of SEQ ID NOS: 24, 41, 101, 157, 291, 305, 315, 341, 63, 116, 134, 136, 151, 384, 404, 308, 213, 367, 188, 251, 202, 315, 367, 397, 256, 382, 169, 23, 291, 324, 330, 341, 353, 188, 379, and 395.

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11. The polynucleotide of claim 8, wherein the polynucleotide comprises a sequence encoding a polypeptide having a functional domain selected from the group consisting of: Ank repeat, basic region plus leucine zipper transcription factors, bromodomain, EF-hand, SH3 domain, WD domain/G-beta repeats, zinc finger (C2H2 type), zinc finger (CCHC class), and zinc-binding metalloprotease domain.

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12. The polynucleotide of claim 11, wherein the polynucleotide comprises a sequence of one of SEQ ID NOS: 116, 251, 374, 97, 136, 242, 379, 306, 386, 18, 335, 61, 306, 386, 322, 306, and 395.

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- 13. A recombinant host cell containing the polynucleotide of claim 8.
- 14. An isolated polypeptide encoded by the polynucleotide of claim 8.
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- 15. An antibody that specifically binds a polypeptide of claim 14.
- 16. A vector comprising the polynucleotide of claim 8.

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18. A method of detecting differentially expressed genes correlated with a cancerous state of a mammalian cell, the method comprising the step of:

detecting at least one differentially expressed gene product in a test sample derived from a cell suspected of being cancerous, where the gene product is encoded by a gene corresponding to a sequence of at least one of SEQ ID NOS:4, 9, 39, 42, 52, 62, 65, 66, 68, 74, 81, 114, 123, 144, 130, 157, 162, 172, 178, 183, 202, 214, 219, 223, 258, 298, 317, 338, 379, 384, 386, 388, 1, 39, 52, 97, 119, 134, 172, 176, 241, 288, 317, 357, 362, 374, 9, 34, 42, 62, 74, 106, 119, 135, 154, 160, 260, 308, 323, 349, 361, 369, 371, 379, 395, 381, and 400; wherein detection of the differentially expressed gene product is correlated with a cancerous state of the cell from which the test sample was derived.

- 19. The method of claim 18, wherein said detecting step is by hybridization of the test sample to a reference array, wherein the reference array comprises an identifying sequence of at least one of SEQ ID NOS:1-844.
- 20. The method of claim 18, wherein the cell is a breast tissue derived cell, and the differentially expressed gene product is encoded by a gene corresponding to a sequence of at least one of SEQ ID NOS: 4, 9, 39, 42, 52, 62, 65, 66, 68, 74, 81, 114, 123, 144, 130, 157, 162, 172, 178, 183, 202, 214, 219, 223, 258, 298, 317, 338, 379, 384, 386, and 388.
- 21. The method of claim 18, wherein the cell is a colon tissue derived cell, and the differentially expressed gene product is encoded by a gene corresponding to a sequence of at least one of SEQ ID NOS: 1, 39, 52, 97, 119, 134, 172, 176, 241, 288, 317, 357, 362, and 374.
- 22. The method of claim 18, wherein the cell is a lung tissue derived cell, and the differentially expressed gene product is encoded by a gene corresponding to a sequence of at least one of SEQ ID NOS: 9, 34, 42, 62, 74, 106, 119, 135, 154, 160, 260, 308, 323, 349, 361, 369, 371, 379, 395, 381, and 400.

SEQUENCE LISTING

<110> Lewis T. Williams Jaime Escobedo Michael A. Innis Pablo Dominiguez Garcia Julie Sudduth-Klinger Christoph Reinhard Klause Giese Filippo Randazzo Giulia C. Kennedy David Pot Altaf Kassan George Lamson Radoje Drmanac Radomir Crkvenjakov Mark Dickson Snezana Drmanac Ivan Labat Dena Leshkowitz David Kita Veronica Garcia William Lee Jones Birjit Stache-Crain

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tgctctaatt gggtggaagg tgctgtatct aacttgtgtt cctcctaagg ttatgtccta
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aggagteegg gagatgtgtg atgeatgtga ageaacattg tttaacatte actgggtetg
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ccaaaaatgt ggatttgtgg tctgcttaga ttgttacaag gcaaaggaaa ggaagagttc
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gtcctaatcc caggaacctg tcaaaattac cttgtatggc caaaggggct ttgcagatgt
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gaagetgtga acagtaccat cagtaacatt ttatggacag etetgatggt ttttatacca
                                                                      180
eggeaetett ettacetttg ggggaageta tetggagtta tgaetgatgt gtaaagtggt
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ccttgccagg gccagagctg gtaacagcgg ggcagcaggg tgggtagcct ctaccagcca
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gggcagtccc tgaggggcca gcaggggggc tgactgccta gtggctcaac ctcctgaacc
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ccccatttta caggtgaaga aactgagtct ctgagagacc aacttttcca aggtcacaca
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aggectggeg cagtgactea tgeetgtgat eccageaett gggaggeega ggegggtgga
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tcatttgagg ccaggagttc gagaccagct tggccaacat gatgagaccc cgtctctatt
                                                                      240
                                                                      300
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caaannaagg anganngnta ggngngaaaa anaanaacaa anggggaaaa ngggaaaaaa
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                                                                      240
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tgctctggtc aaaaccaagc acaccatagc cttaactgaa tatttaggaa atctgcctaa
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gaagteette aaagettagt tgatgatggt atggttgact gtgagaggat eggaaettet
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gectgggage acctetttge ttttcacace aaaccaaaac tggegagage cectectage
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ggccagagca aaggaaaacc tcttgtttta aaaaaatttt tttcagagtg ttttggggag
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gtttattaat tctatttaat caaggaaaat aacttcagat tccataaagt ttcagtttat
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ttttagttta ctactaggtg agatagcaca ttacatactt ttactatcaa atattatttt
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totgactatg gaaatgatat tagacaaaaa gcaacttcaa gtgggtttot tatttgagtt	240
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tgagetteag tteeettaae tagaaaaata gaacaggeee ggtgeggtgg eteataeetg taateeeage aetttgggag getgaggegg gtggateatg aggteaggag ateaagaeea	240 300
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cttcaaattt caggccatct atttttaatt taatcccgtt caagtacttg attgttatac	300
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aacgaattgc acaaagtacc catttaaaat ttacatgcac agttcattgc cacctttctt aggcctatgc atagttaata aggttataat ctactcaaca tggaaaatgg agcctatttg	240
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cggagagaat atcagcgaca ggactacatg gatgccatgg ctgagaagca aaaattggat	240 300
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tttatccaag attagatgtg attactattt aataataatt tagtcctcac acttacaaac
cacttacaat accagcatge ttetateact gtaattetat teaattetea ggeecatgag
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agatccagca tgggattagg tactgaaatg gattagaact aaaagtcact agaatttaga
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aattgagaac catgagagtg gatgcaatga cttgttgctt gattgaaaaa taaattaata
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gacagtggat tacagtttgt gtggcaaagt ccaagttgtt acactgtgct ttaaaaaaaaa
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                                                                      180
gettacetgt etggeteage ttgggeaagg getgggeeat atgtgeteag ggaegtgett
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catccatgtc ggagtctctc tccatcccag cttccctgaa cgacgcqqct ttqqctcaqa
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tgaacagtga ggtgcagctc ctgactgaaa aggccctgat ggagcttggg ggtgggaagc
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tttcattgcc agatcatgaa atccaaagaa actttaaaga agatgagttg tgtaaatgga
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aagagagcaa ggaaaagaac tagtatggaa acagcacttg cccttgagaa gctattcccc
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aattettget gagteaagag tgtaaataaa agaaatggea ggacteatat tatteagttg
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ttctaaaata ggactttcat attattaaaa cctcaaaaga tgatccaccc aggatgaaca
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ticatitic acaaactiga aattagccig ctaatigtaa agtigtitta ataatgciga	240
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agaatttaaa ataattttga acgaatttat tttcccctca gtttttgagg gcattaaaaa
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agctggcacc acccagatca					180

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actgactcag tgcaagaaga cagcttcgac tccctgtgat ttcatctctg accaatccgc actcctggct cactggcttc cccaacccat gaagttttcc ttaaaaactc tgctcccgaa	240 300
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qctcctccqt cqtqgatttc gcggcgatcc ccccggcagc tctttgcaaa gctgcttgaa
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tetgeacetg accaeactee ctacteaggg ctagtetgtt ctteeeggac atettetggt
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nnnnnnnnn nnnnnnnnc atcatgtccn ntgcatggct acctatccca tatttnatnt
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cctatcaaac gagtatataa aaaatttgat ccagttqqaq aqattttaaa aatqcaqqat
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tgeteccaeg teaegggeat ettegeegee eecceageee cagecaecae eteeegeage
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caggeggete agetatgeca egaeggttaa catecaegtg ggeggggtg ggeggetgeg
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aatcacataa gattaaaaat toottootoa gttgoactaa coacgtttot aqaqqogtoa
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ataaagcage tecagtitea ggacetegae tggatittga teetgacati gitgeagete
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tgaacttcca ggagtatgtc accttcctgg gggccttggc tttgatctac aatgaagccc
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tgagccctgc ggcccacctg atgtttacgt gtgtgtgtga gggggggcnn nnnnnnnnn
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nnnnnnnnn ngtnatangc ttaacanatg nanagncnac tnactnctga ttntttatnc
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tagtggagaa ggggatgata gtttaaggat aggtggnnnn nnnnnnnngc engenttnac
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ttnatngcnn ctttttcttg atcnacgncn gnnatncnna nnngtntata ntaatncnga
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480

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                                                                      720
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tecagtgate cetttteate etccagtgte tectcaaaag gateagatee etttggaace
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tattagaaaa aaaatttctg gagtgagagt naagangctt aattagtttg tgggcagttt
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tgagacttct ttgactgata gattattgtg aatgtgtttt taaatttcca aatgtttang
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aacagattct gacattgatg atgcagtaag aaactgtgaa attcgagcca tataaataaa
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cttaatgggc agcattccgt cgtcacaagc gggcattcat cctttcatca atagcggca
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360

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gaagaaggcn ggggagaatt gatganttgg ttcaactgcc aaagtgtgtg cantcactca
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cacattttan qqqcattqqq taatcctqaq attttactca ntaaatcctq atqqtactqq
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antnncttga gngggatgaa ccctaananc ctggccctnn tnccnctttc aaggccnagn
                                                                       540
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nnnactatgn naaatattct cacatntaca naaaaagnag gnnccnnggt ncttnaagnt
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